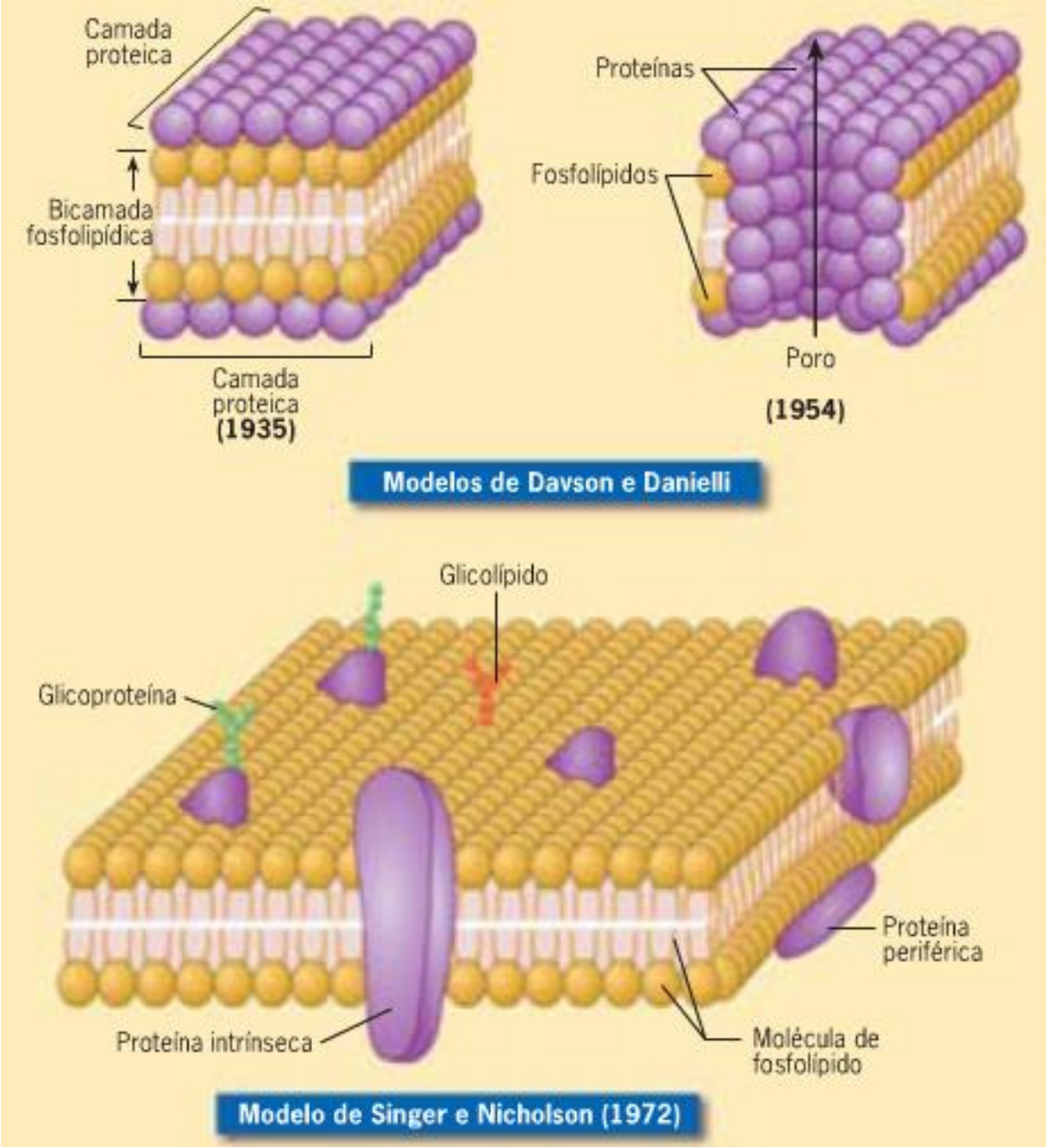
Membranas biológicas

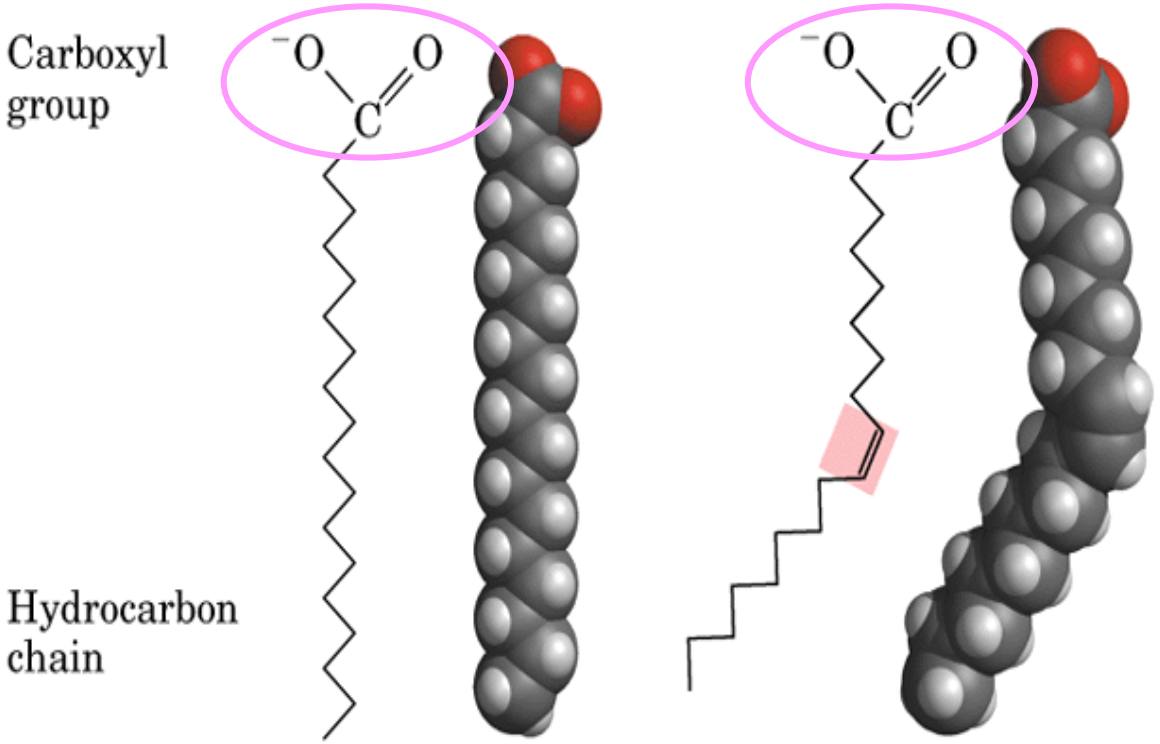
II Semestre, 2025

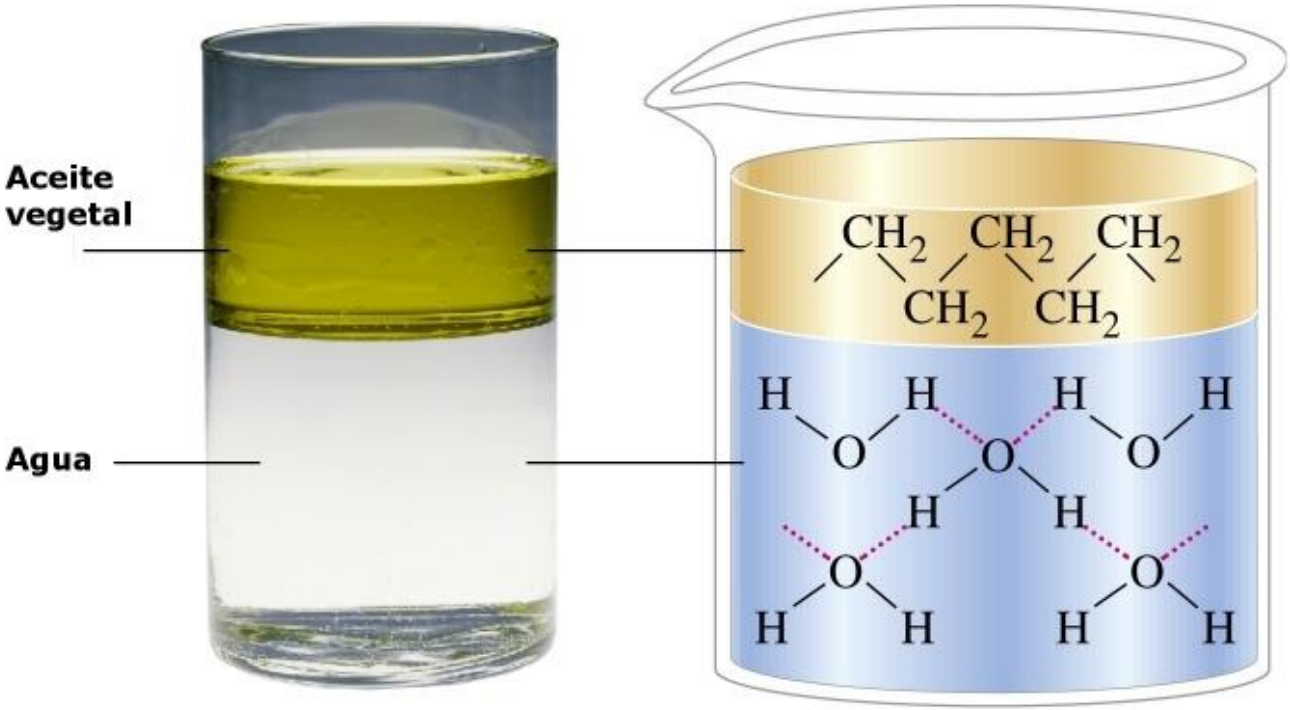
Dra. Carolina Centeno-Cerdas

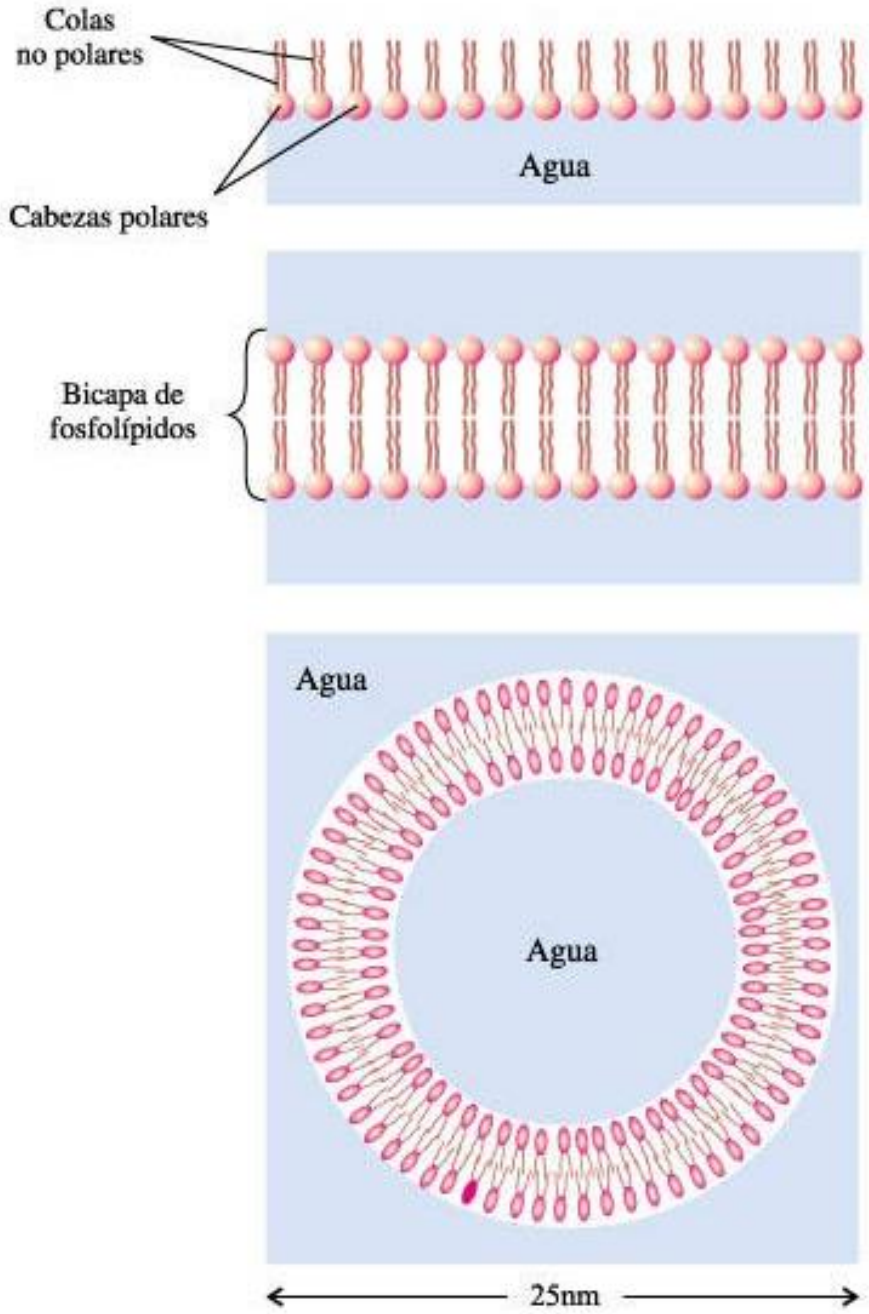
TEC | Tecnológico de Costa Rica

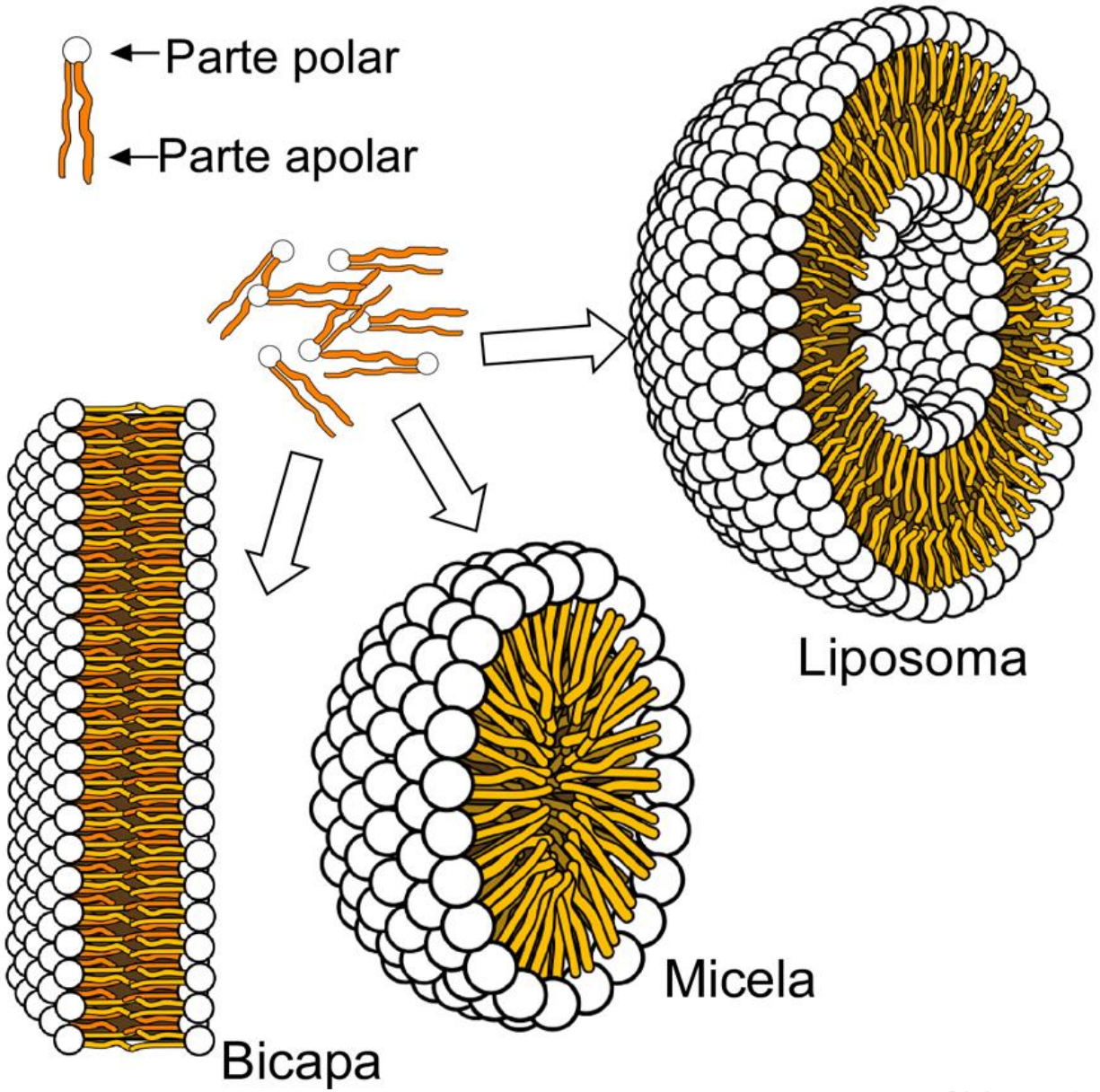

Camada proteica
Bicamada fosfolipídica
Camada proteica
(1935)
Proteínas
Fosfolípidos
Poro
(1954)
Modelos de Davson e Danielli
Glicolípido
Glicoproteína
Proteína periférica
Proteína intrínseca
Molécula de fosfolípido
Modelo de Singer e Nicholson (1972)

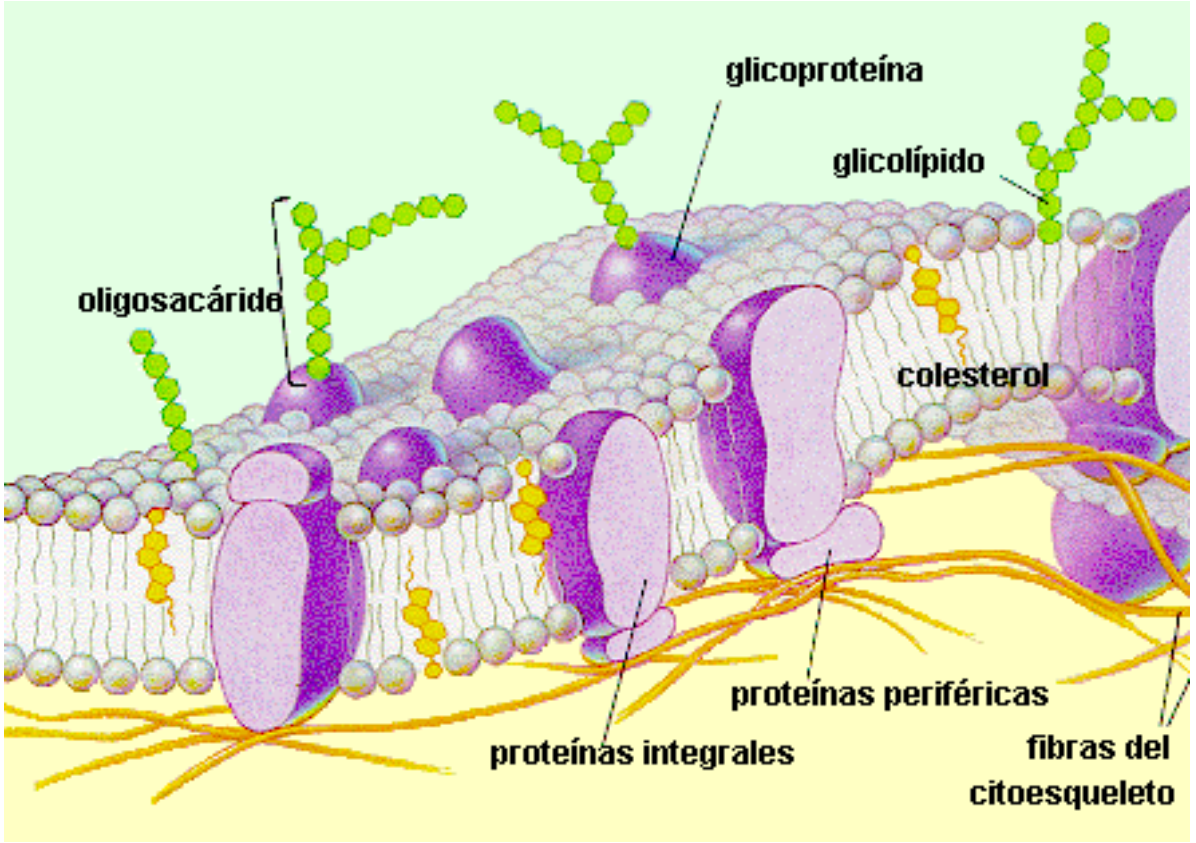
Solubilidad de los lípidos

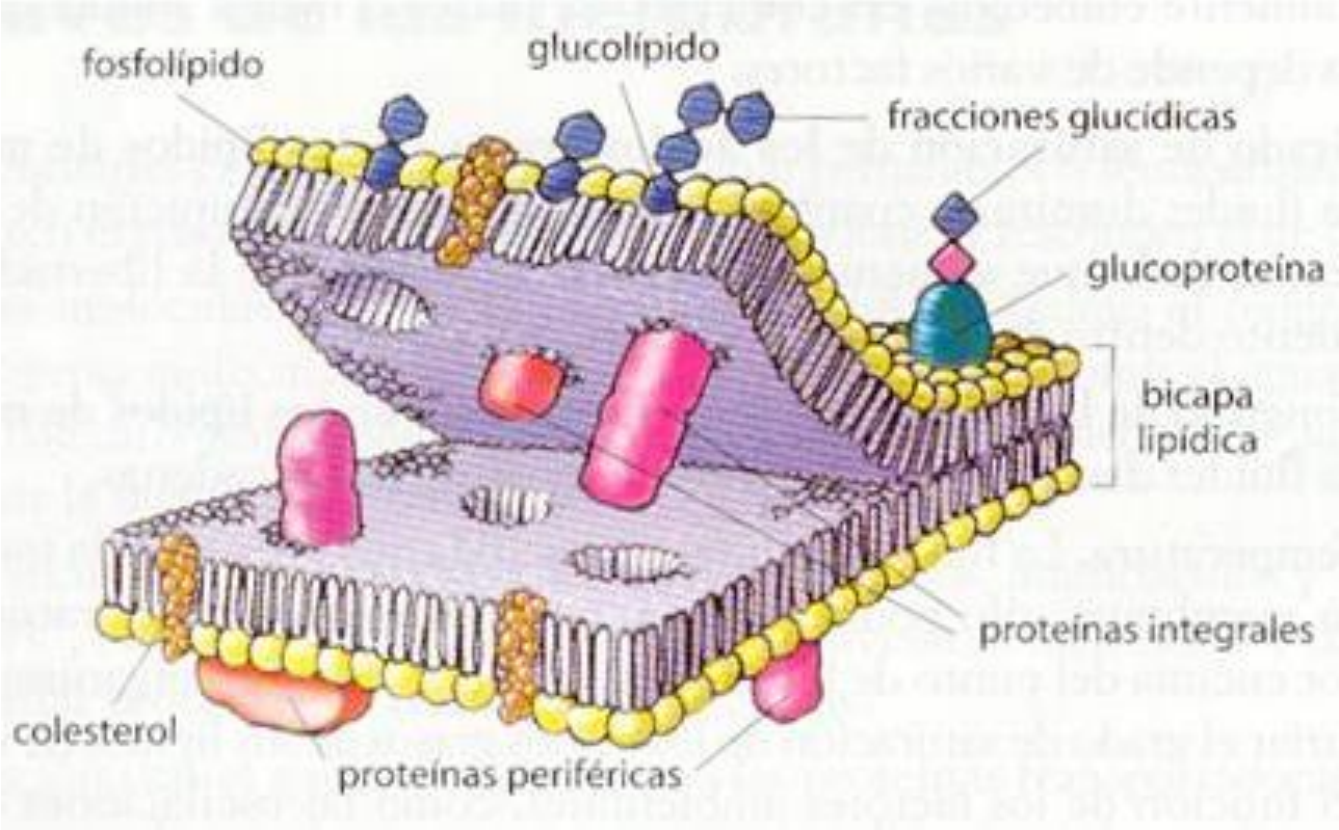





Colas
no polares
Agua
Cabezas polares
Bicapa de
fosfolípidos
Agua
Agua
25nm


Parte polar
Parte apolar
Liposoma
Micela
Bicapa


glicoproteína
glicolípido
oligosacáride
colesterol
proteínas periféricas
proteínas integrales
fibras del citoesqueleto


fosfolípido
glucolípido
fracciones glucídicas
glucoproteína
bicapa lipídica
proteínas integrales
colesterol
proteínas periféricas

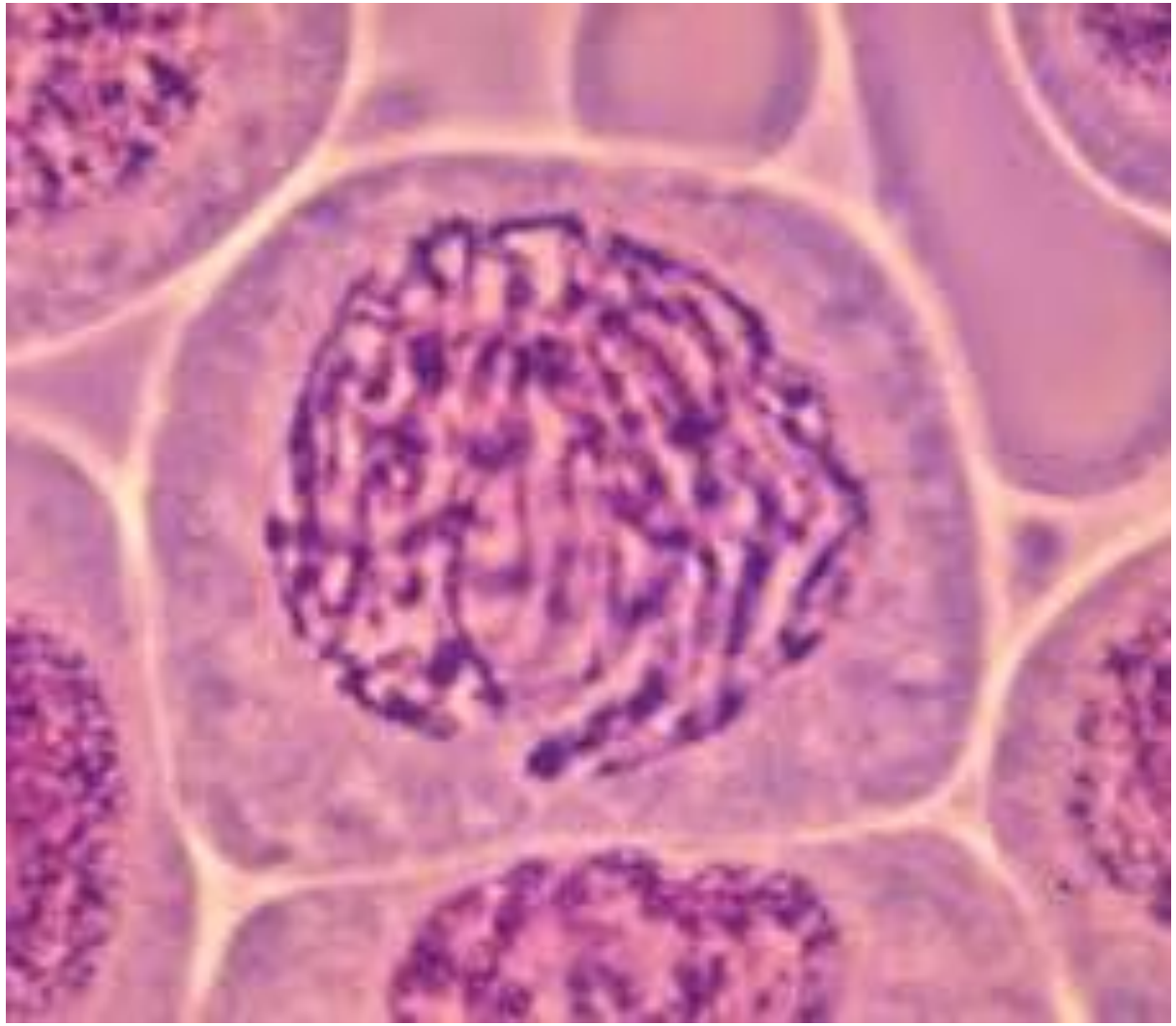
Membranas biológicas

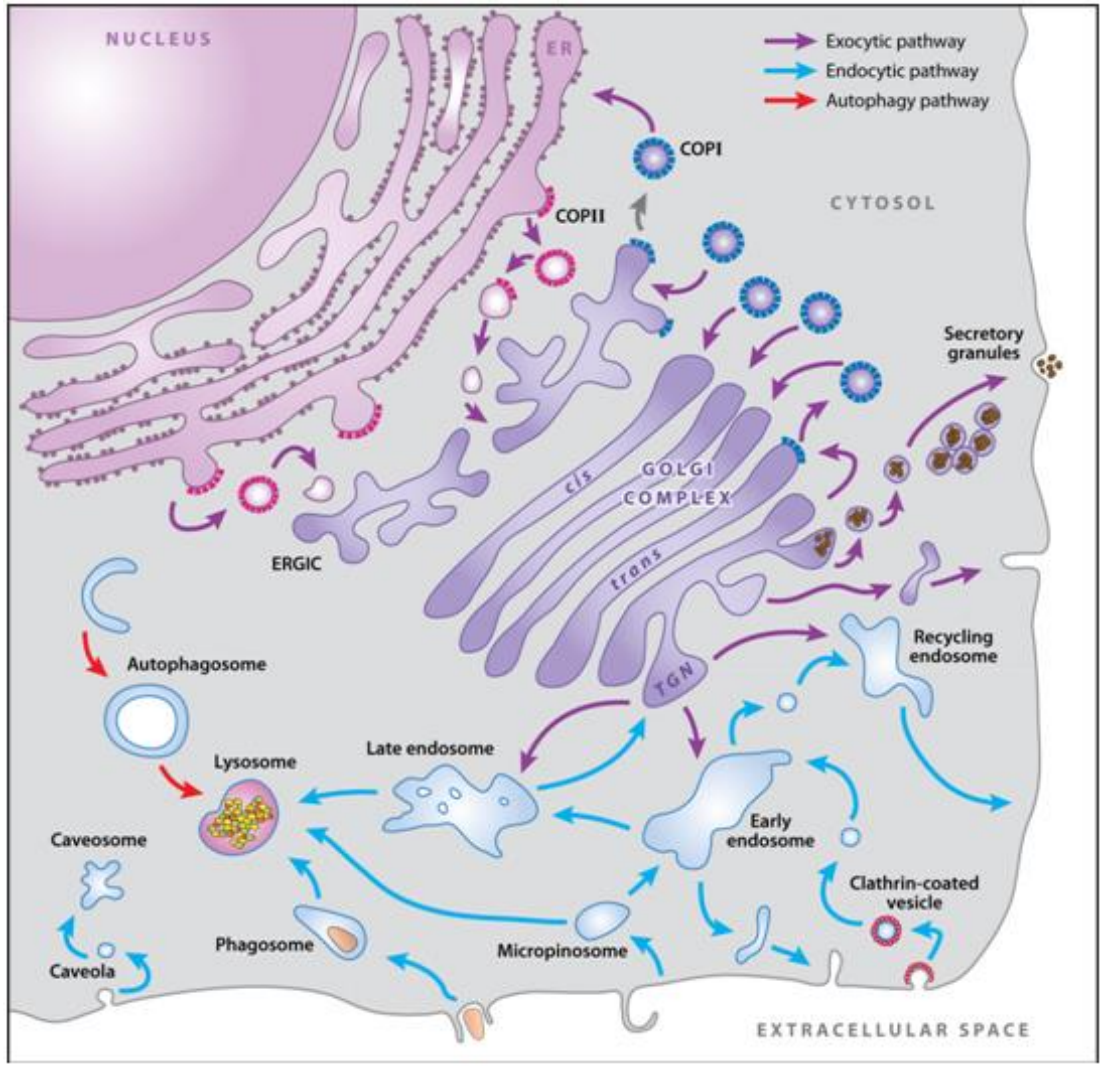
Funciones

- Compartimentalizar
  - “Transportar”
  - “Catalizar”
  - “Comunicar”
  - “Identificar o discriminar”
  - “Unir o sujetar”
  - “Ingerir y excretar”
  - Generar y mantener el potencial electroquímico

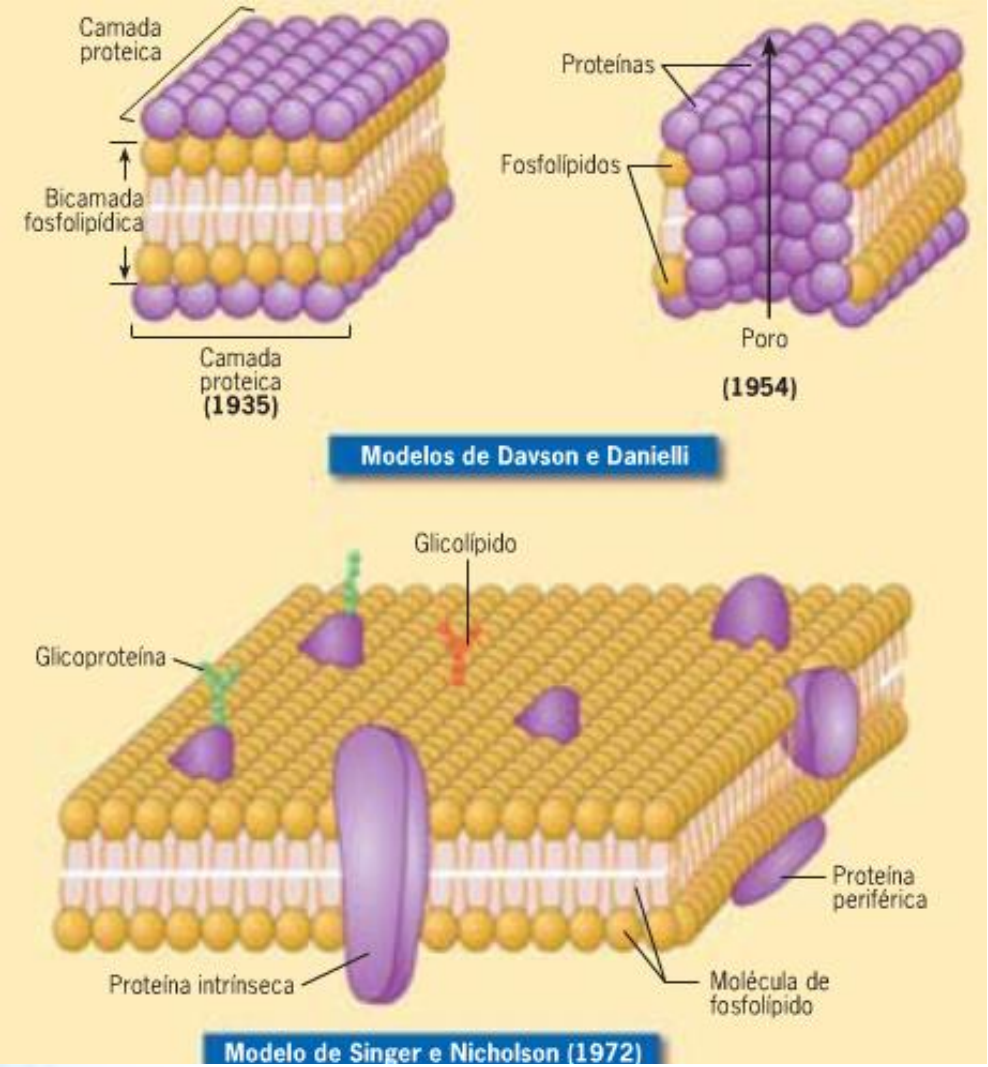
Propiedades

- Impermeabilización
- Selectividad
- Flexibilidad




NUCLEUS
ER
Exocytic pathway
Endocytic pathway
Autophagy pathway
COPI
COPII
CYTOSOL
Secretory granules
cis
GOLGI COMPLEX
trans
TGN
ERGIC
Recycling endosome
Autophagosome
Late endosome
Lysosome
Early endosome
Caveosome
Clathrin-coated vesicle
Phagosome
Micropinosome
Caveola
EXTRACELLULAR SPACE

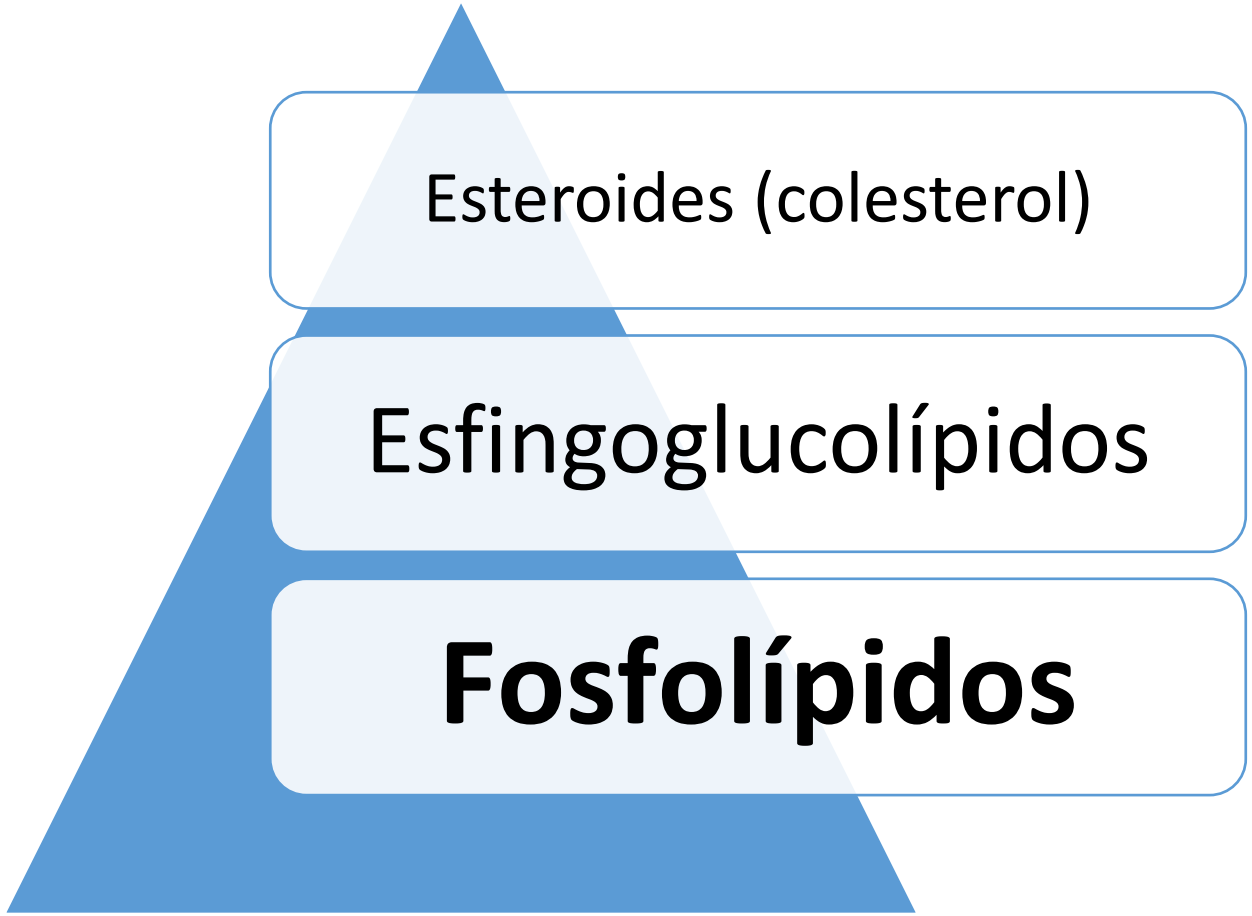
Mosaico *FLUIDO*

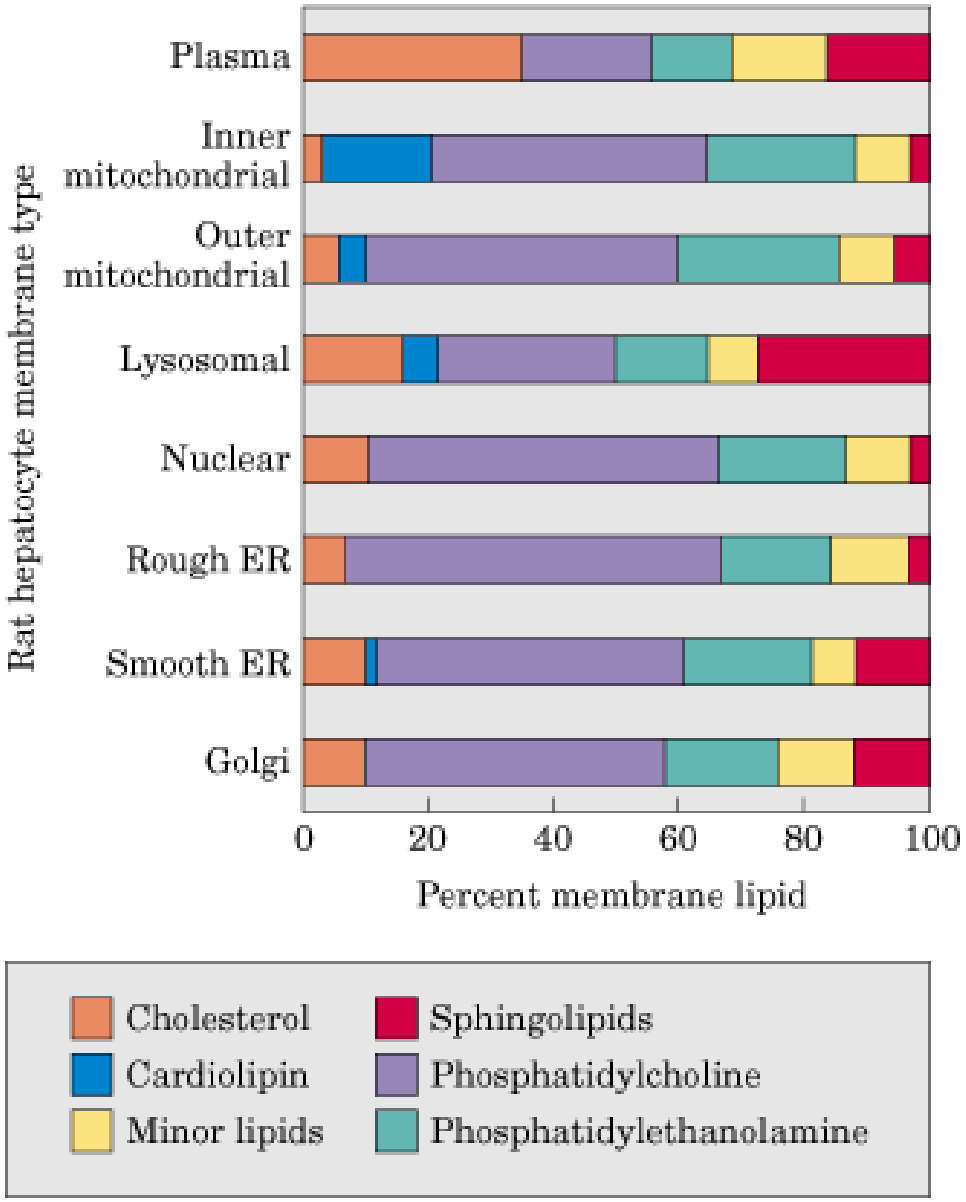


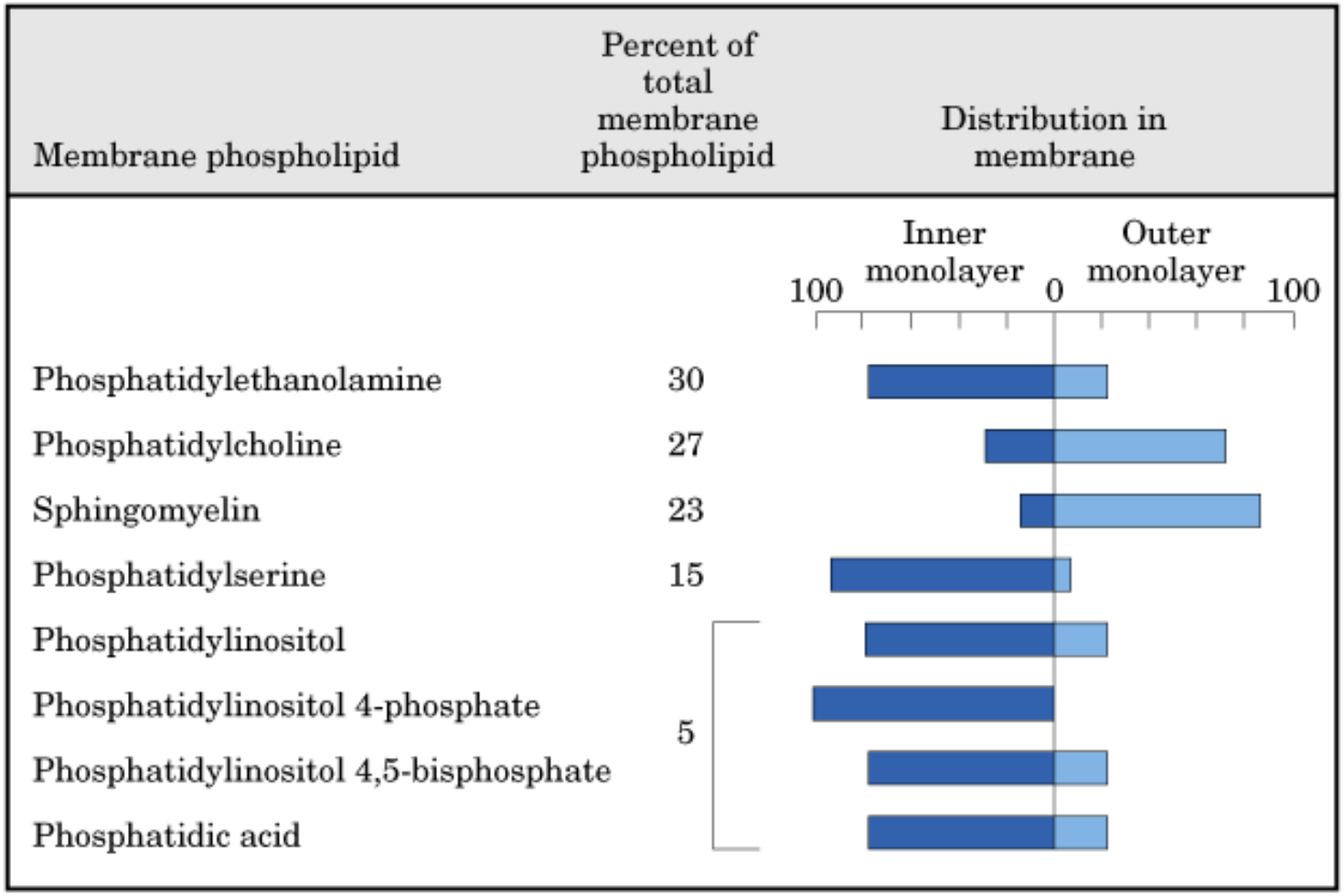
- Fosfatidilgliceroles o fosfolípidos
  - Su naturaleza anfipática posibilita la formación de la bicapa lipídica

- Lípidos (40 a 80% del peso seco)
- Proteínas (20 a 70%, por ej. en la membrana interna mitocondrial)
- Carbohidratos (~8% del peso seco)

Composición de las membranas (lípidos)

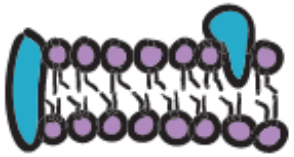






Distribución asimétrica de fosfolípidos entre las monocapas interna y externa de la membrana plasmática del eritrocito

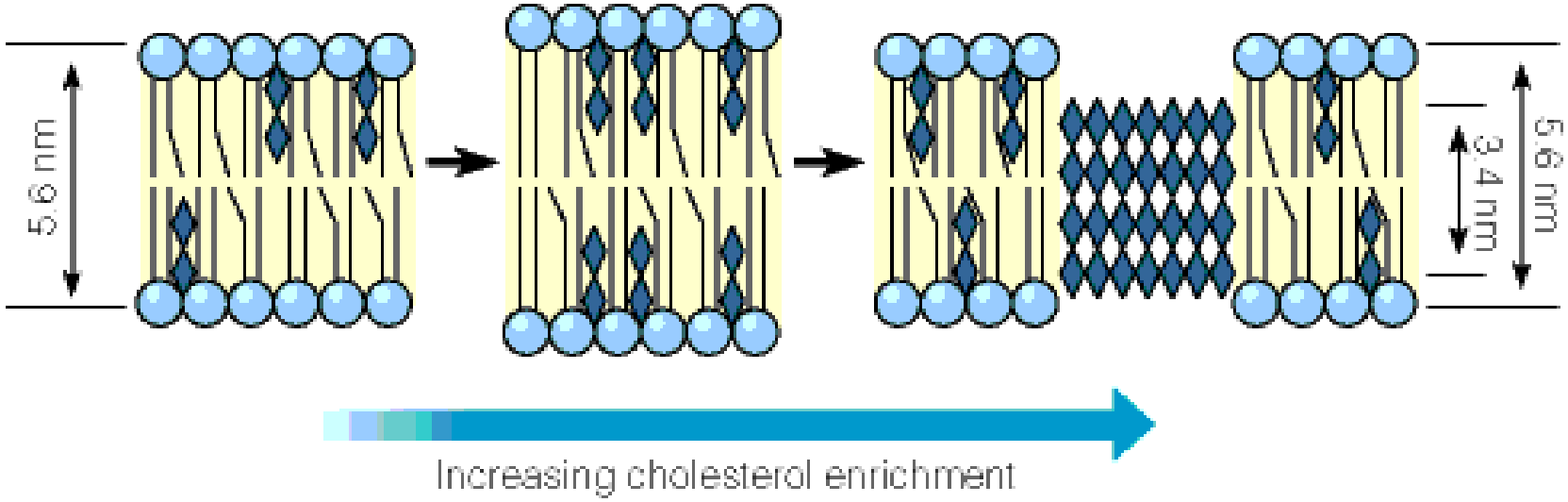
cold

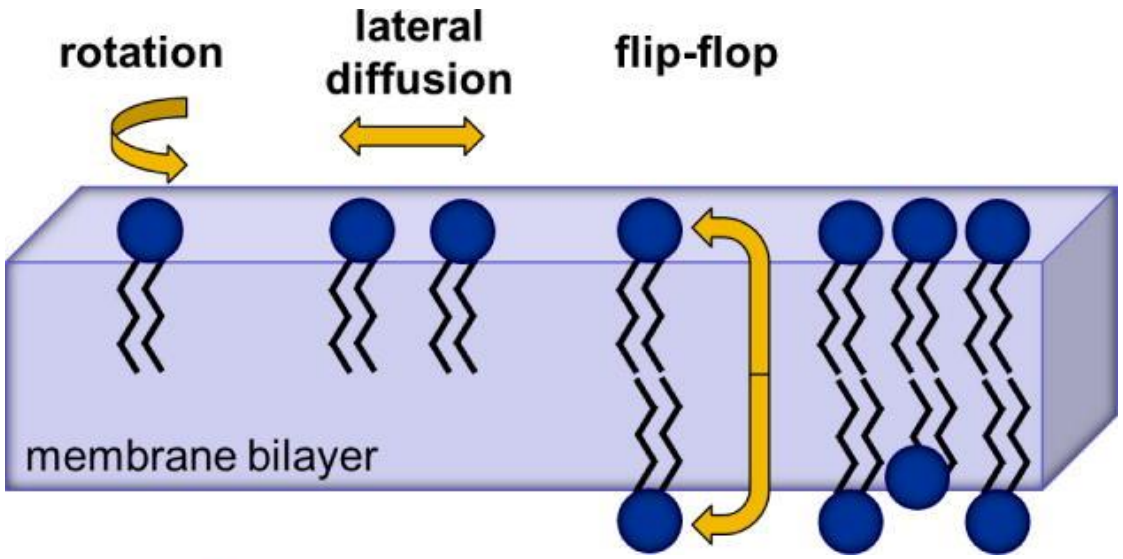


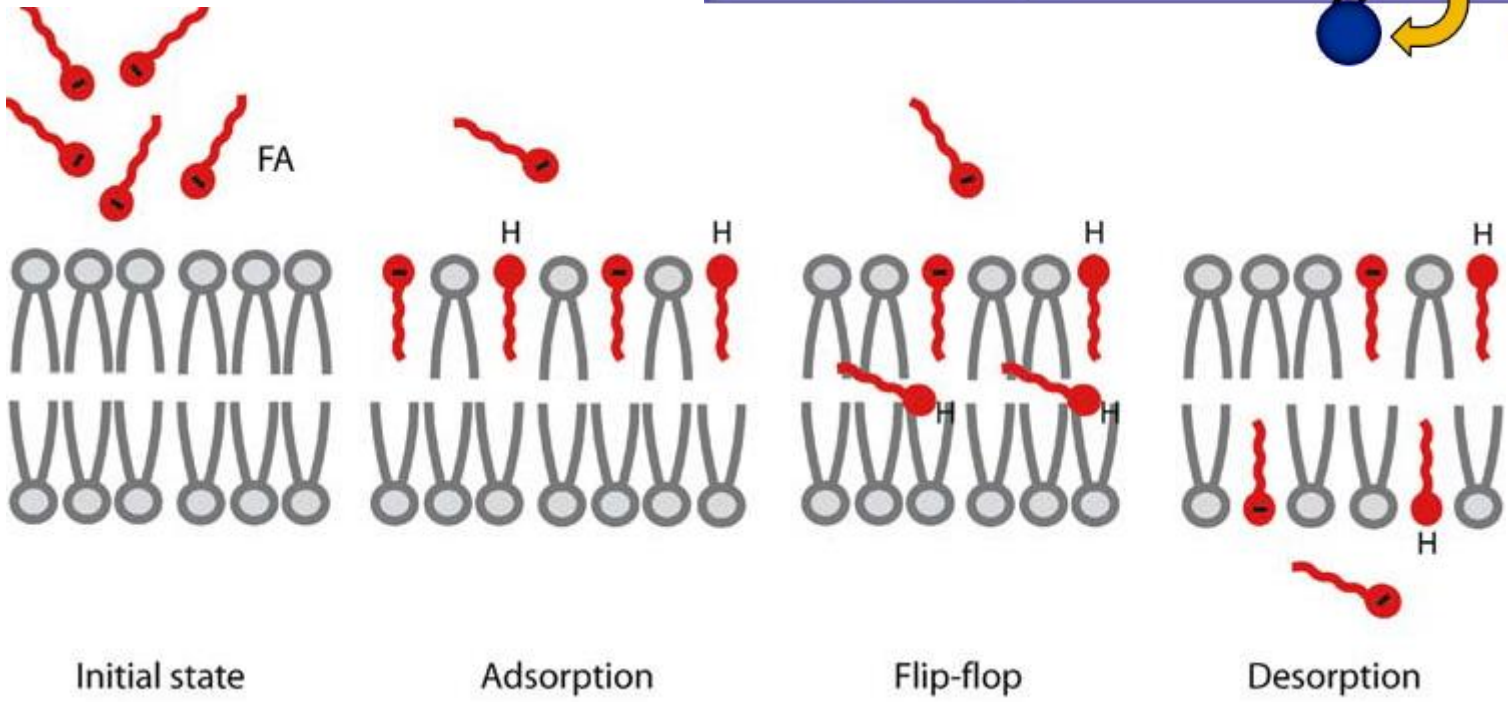
- rigid
- not as fluid/flexible
- may break

hot

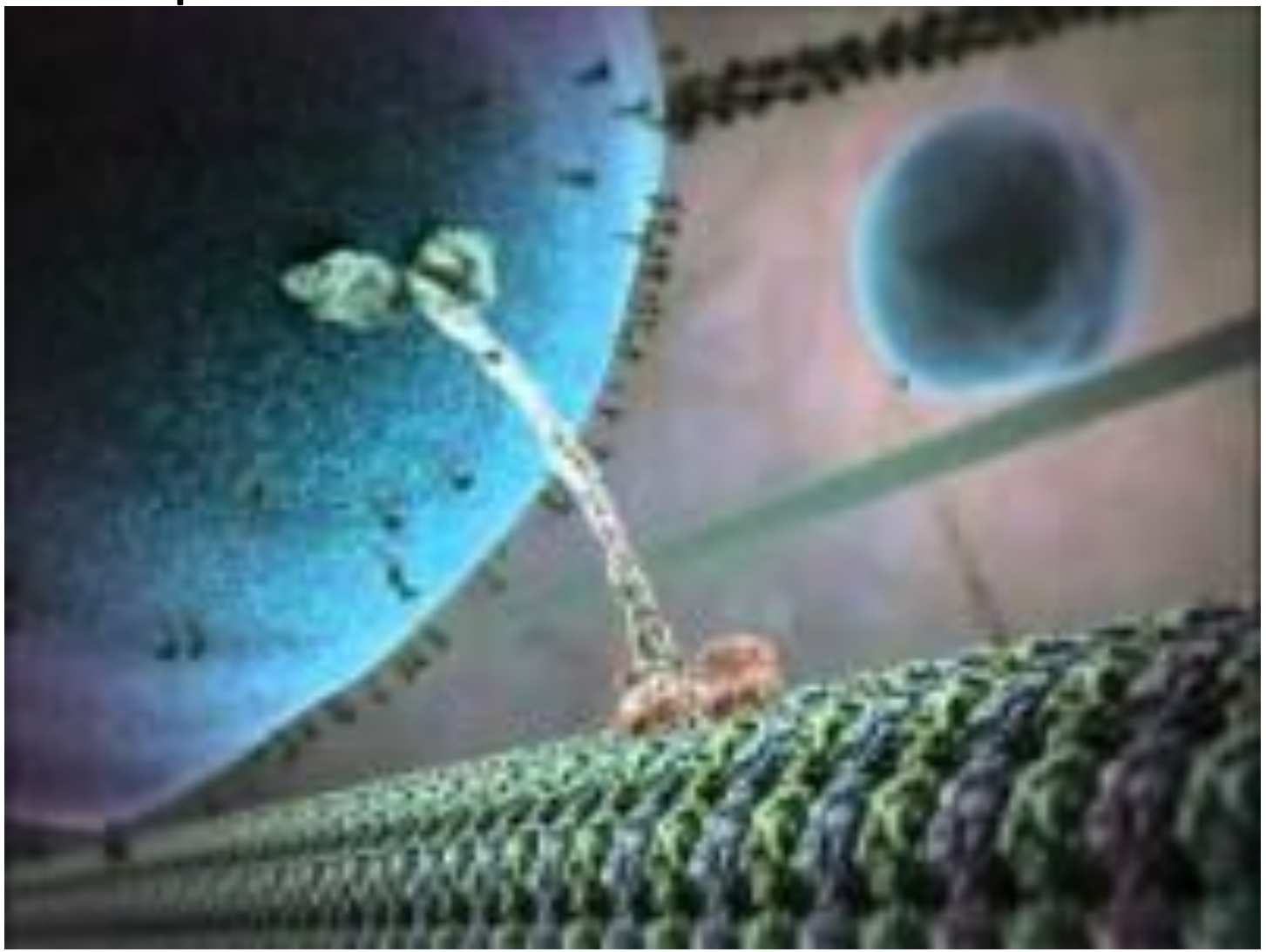
- too fluid/flexible
- won't hold shape




rotation
lateral diffusion
flip-flop
membrane bilayer


FA
H
Initial state
Adsorption
Flip-flop
Desorption

Balsas de lípidos



https://www.youtube.com/watch?v=yKW4F0Nu-UY

Composición de las membranas (proteínas)

- Integrales
- Periféricas
- Unidas a lípidos

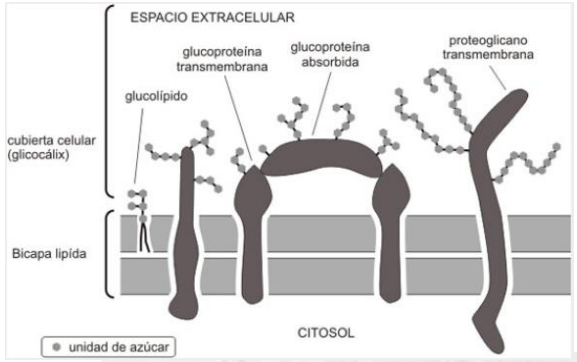
- Proteínas estructurales o de anclaje
- Proteínas receptoras
- Proteínas de transporte:
  - Proteínas transportadoras
  - Proteínas de canal

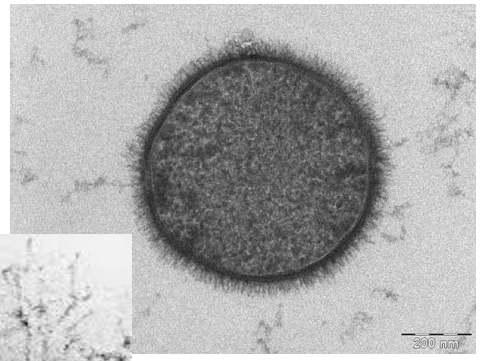
Composición de las membranas (glúcidos)

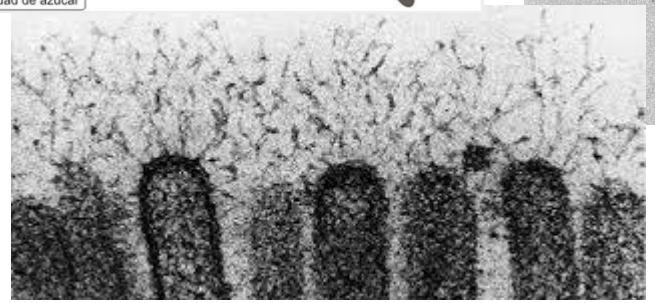
- Participan principalmente en funciones de reconocimiento y anclaje

- Dirigidos hacia el exterior de la membrana unidos covalentemente a
  - las proteínas (glicoproteínas)
  - o a los lípidos (glicolípidos)

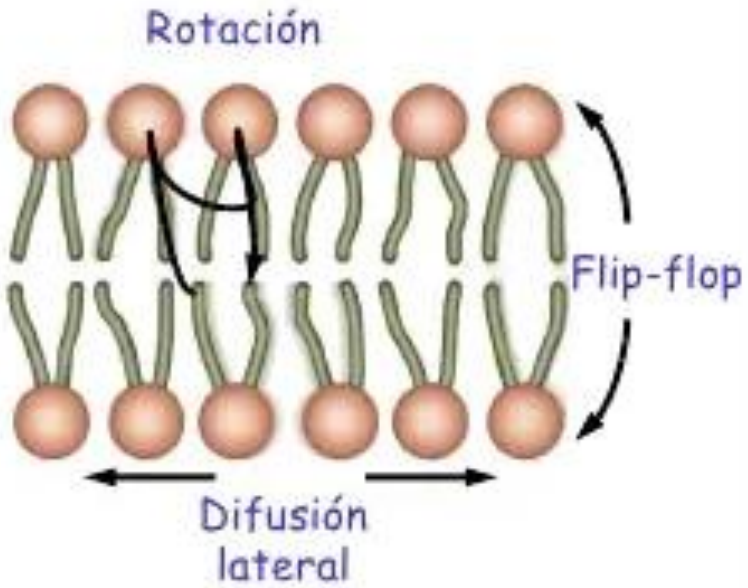
- En conjunto forman el “Glicocálix”



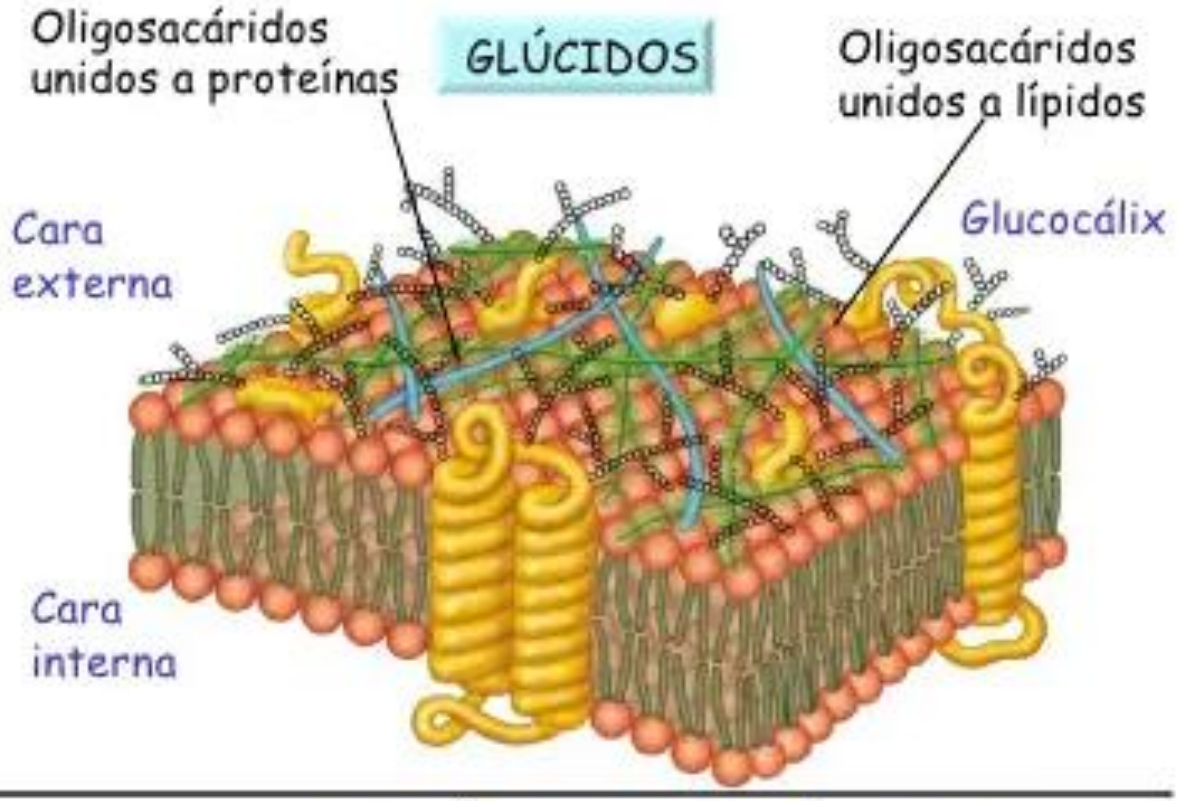




LÍPIDOS *Fosfolípidos, glucolípidos y esteroles.*

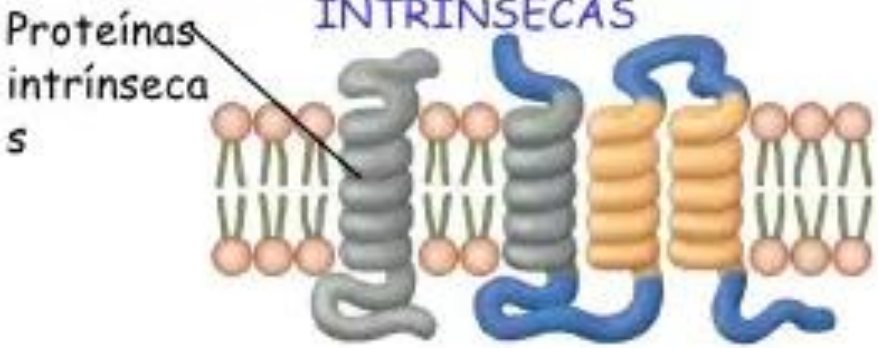


GLÚCIDOS

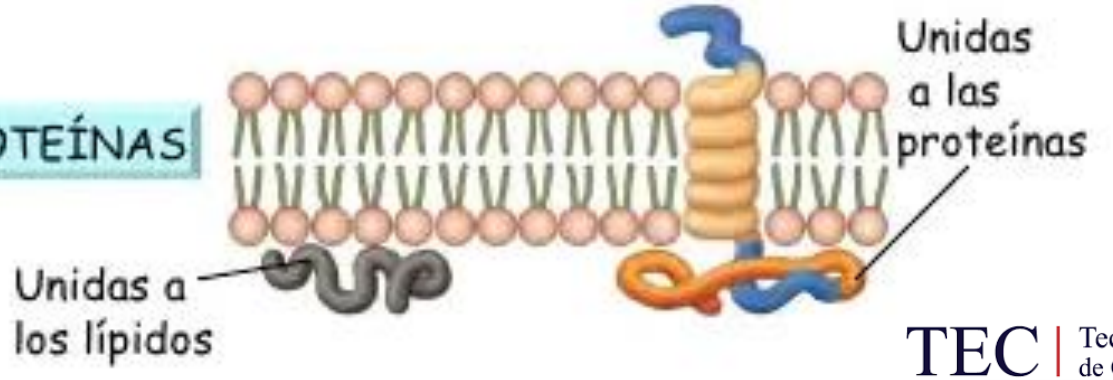


PROTEÍNAS

TRANSMEMBRANALES O INTRÍNSECAS



PERIFÉRICAS O EXTRÍNSECAS



Transporte a través de membranas

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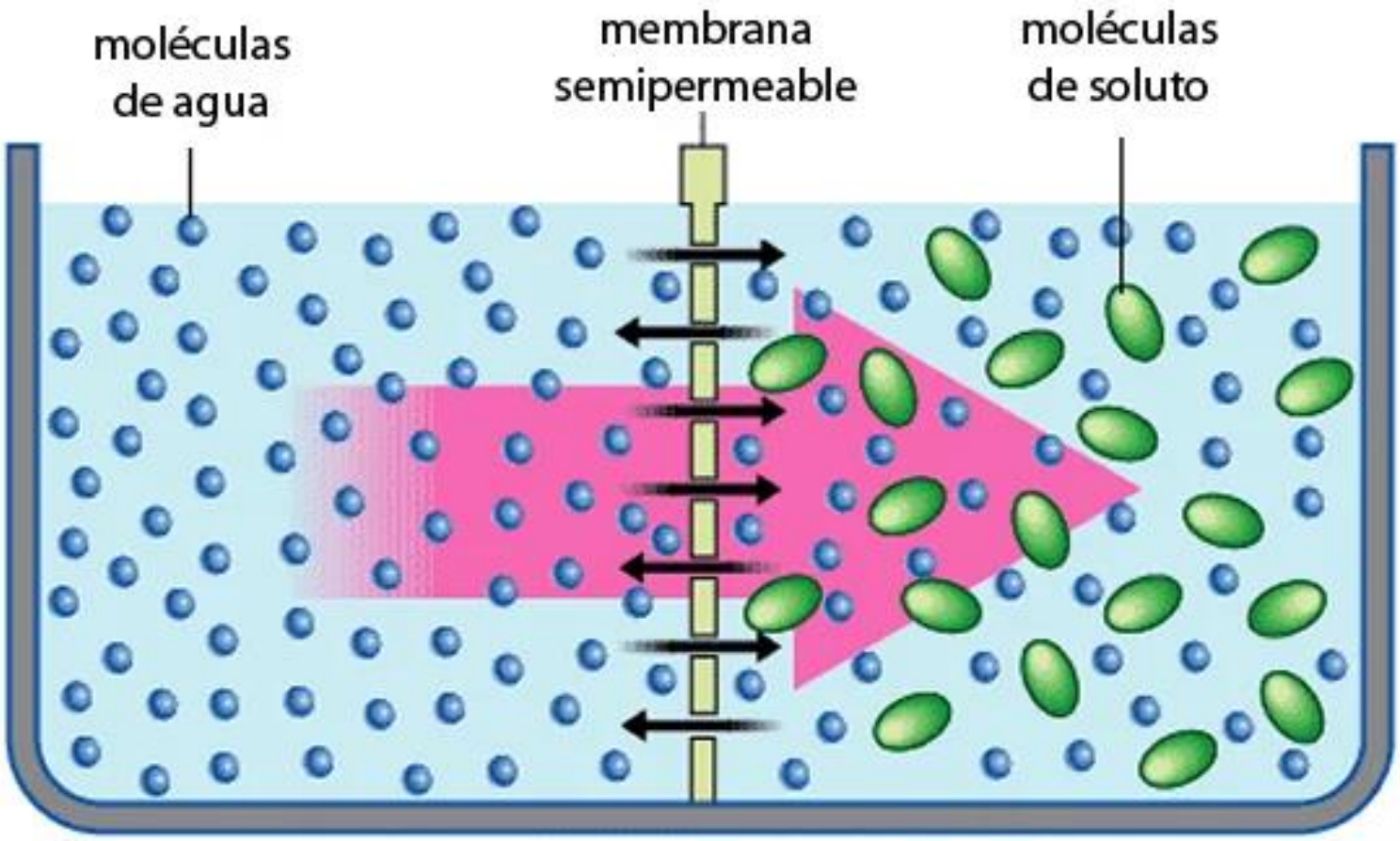
Difusión

- Flujo neto de átomos, iones u otra especie de una región de alta concentración a un área de baja concentración hasta obtener una distribución uniforme

- Es un fenómeno estrictamente físico, el compuesto que pasa no interactúa con ninguno de los componentes de la membrana

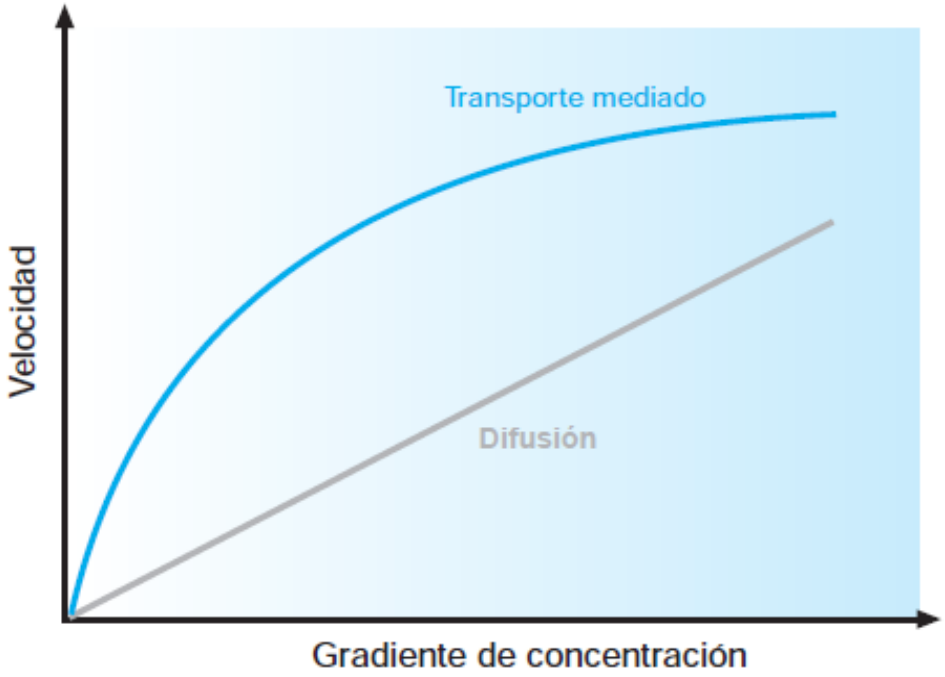
- Normalmente, sólo pequeñas moléculas lipídicas, ciertos gases (O_2, CO_2) y el agua atraviesan las membranas por difusión

Difusión *vs*. Ósmosis



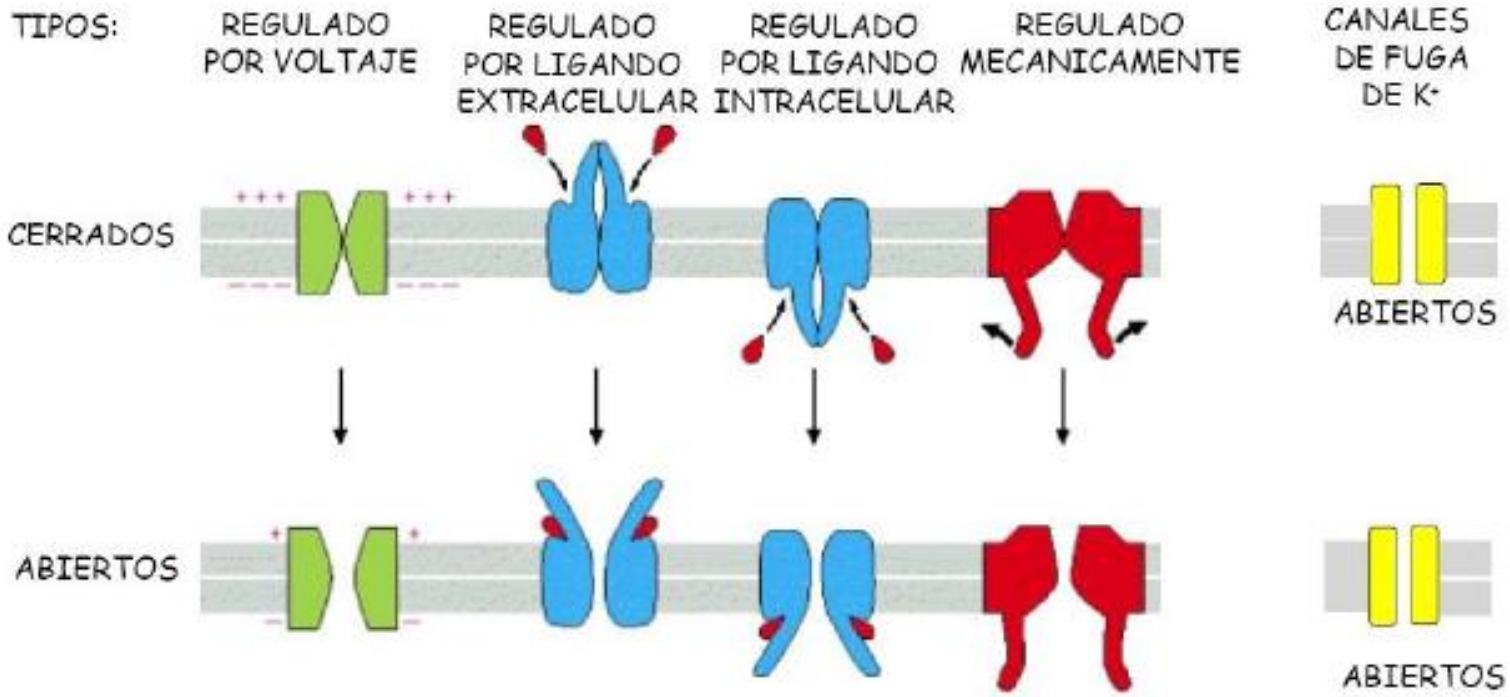
Difusión “facilitada”

- “Transporte mediado pasivo”
  - Transporte de equilibrio
- Participan moléculas estructurales (proteínas):
  - Sistema de transporte, transportador, portador



Canales iónicos

- Pueden ser selectivos (específicos) o “no selectivos” (inespecíficos para iones o para cationes)
- Pueden ser activos o pasivos



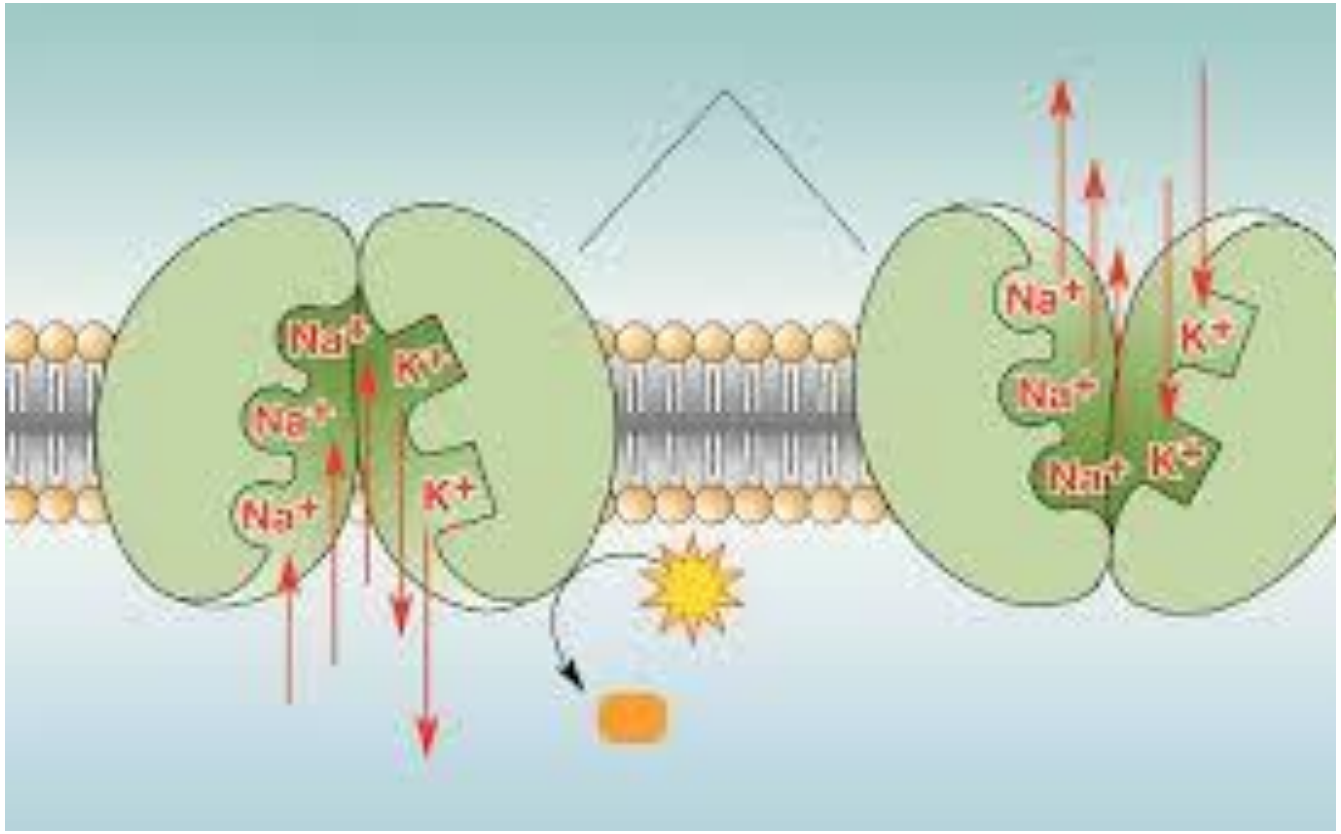
Transporte activo

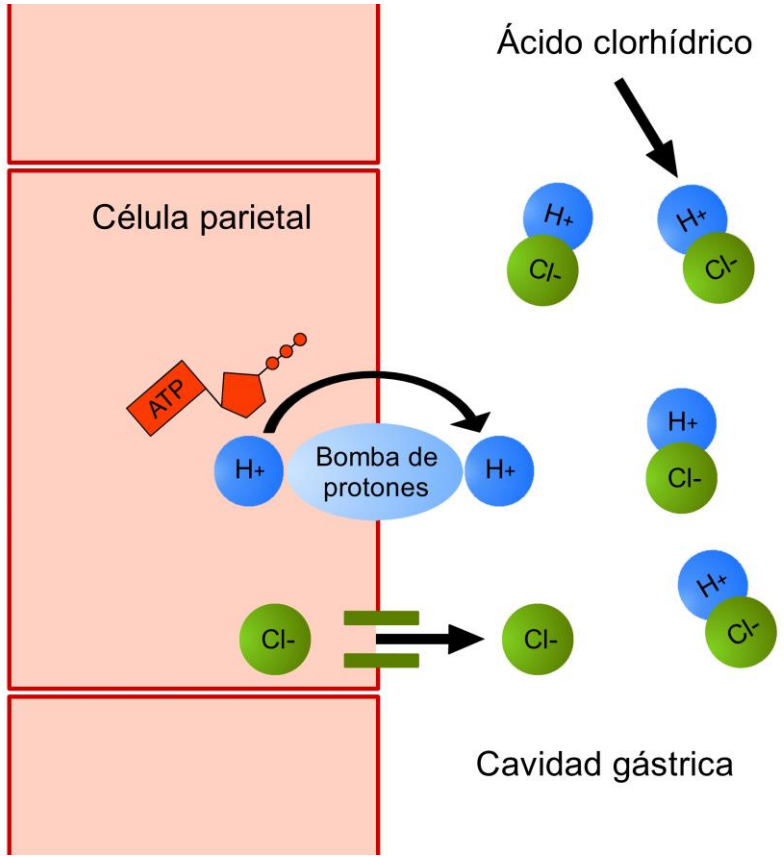
- Ocurre en contra de gradiente

- Depende de energía metabólica:

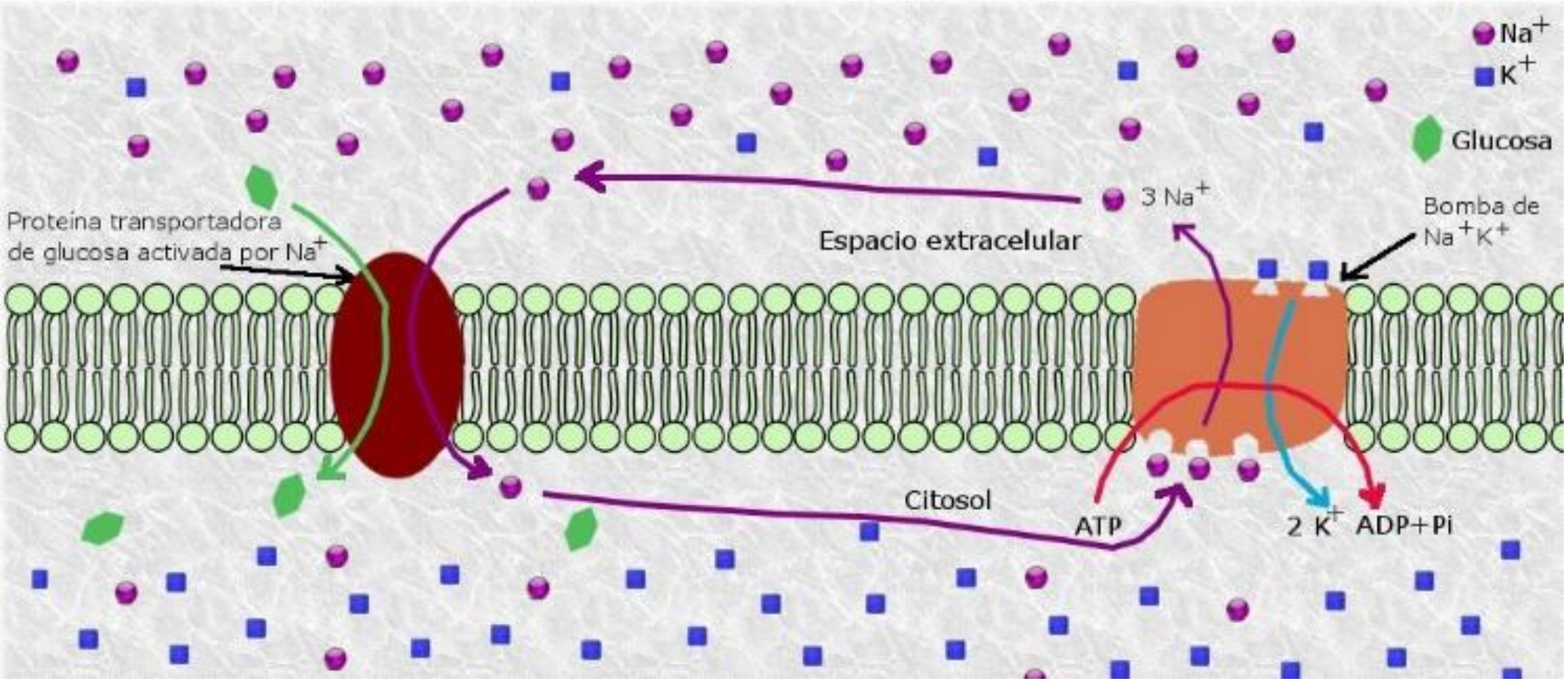
  - Transporte activo “primario”: si la dependencia es directa
  - Transporte activo “secundario”: si la dependencia de la energía es indirecta

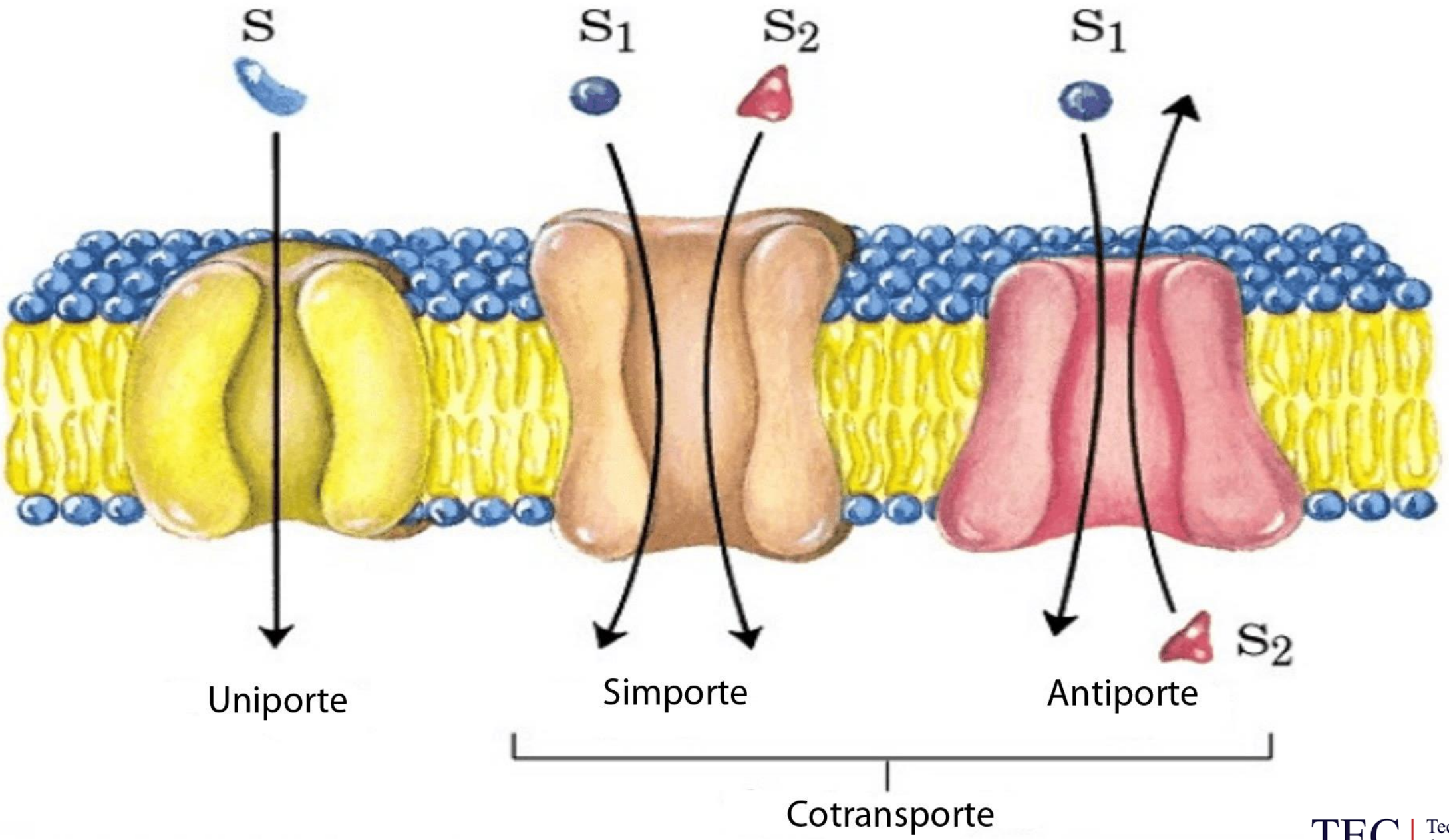
Transporte activo (“primario, normal”)





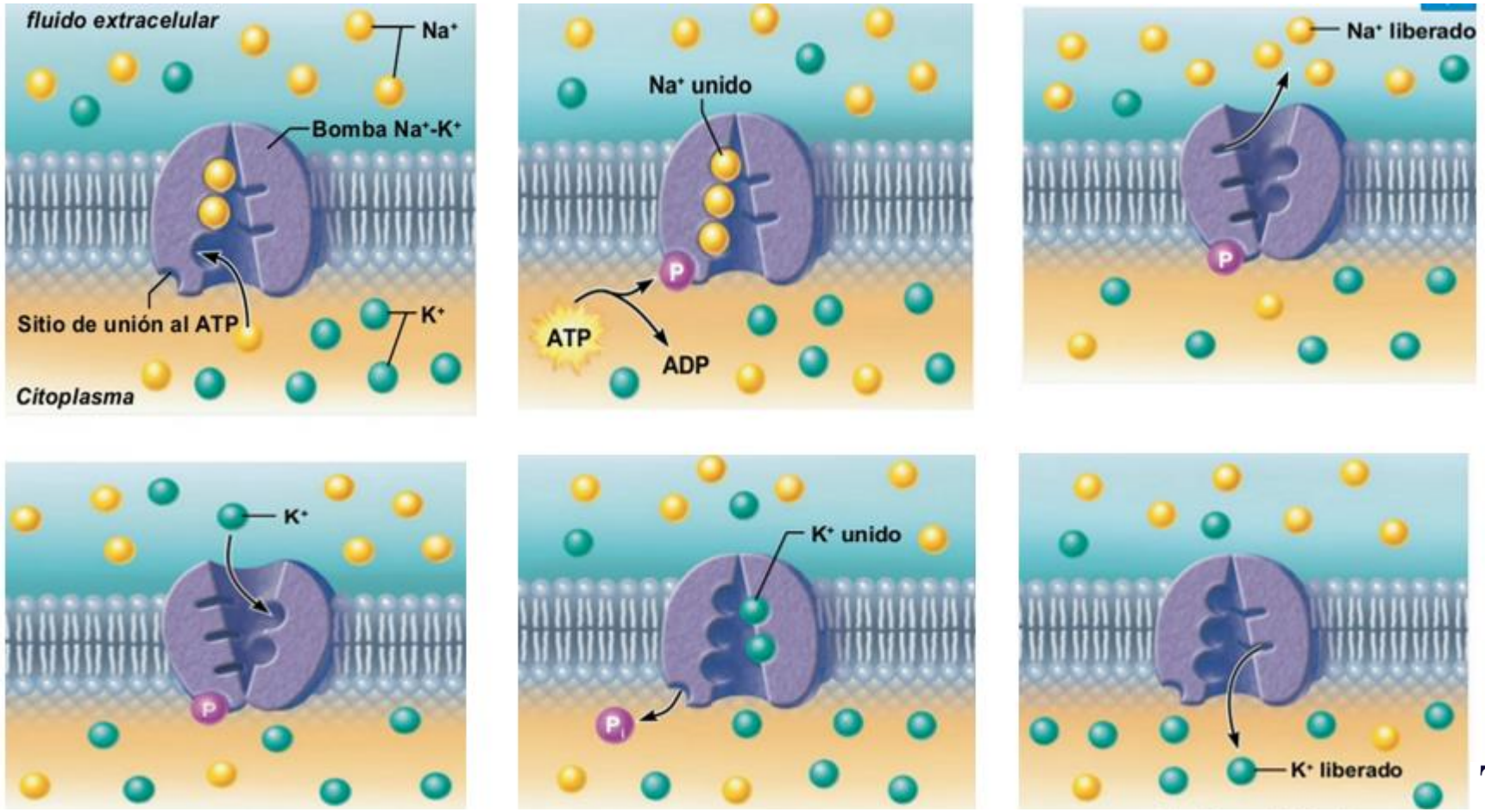
Transporte activo secundario

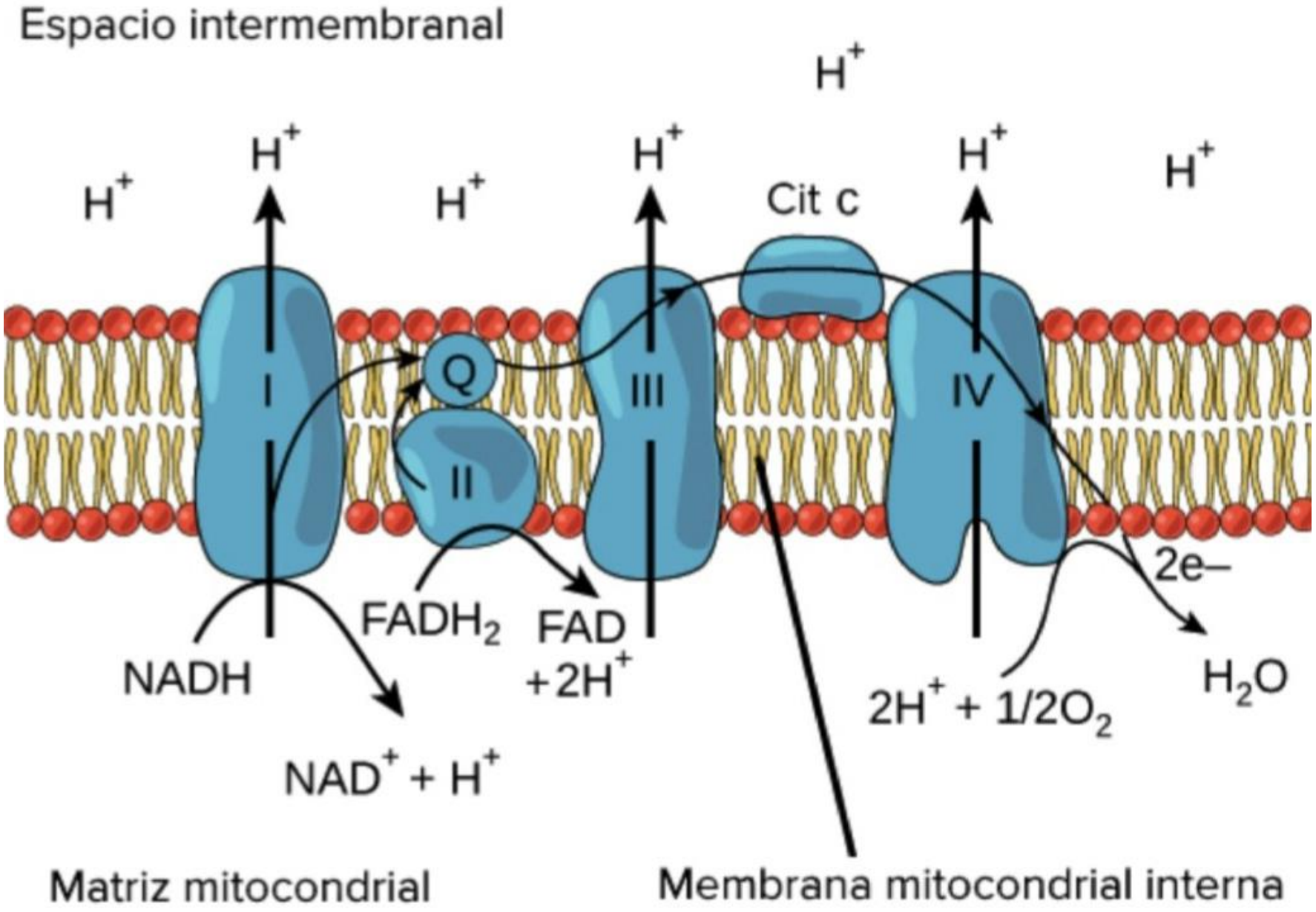



S
S_1
S_2
S_1
S_2
Uniporte
Simporte
Antiporte
Cotransporte

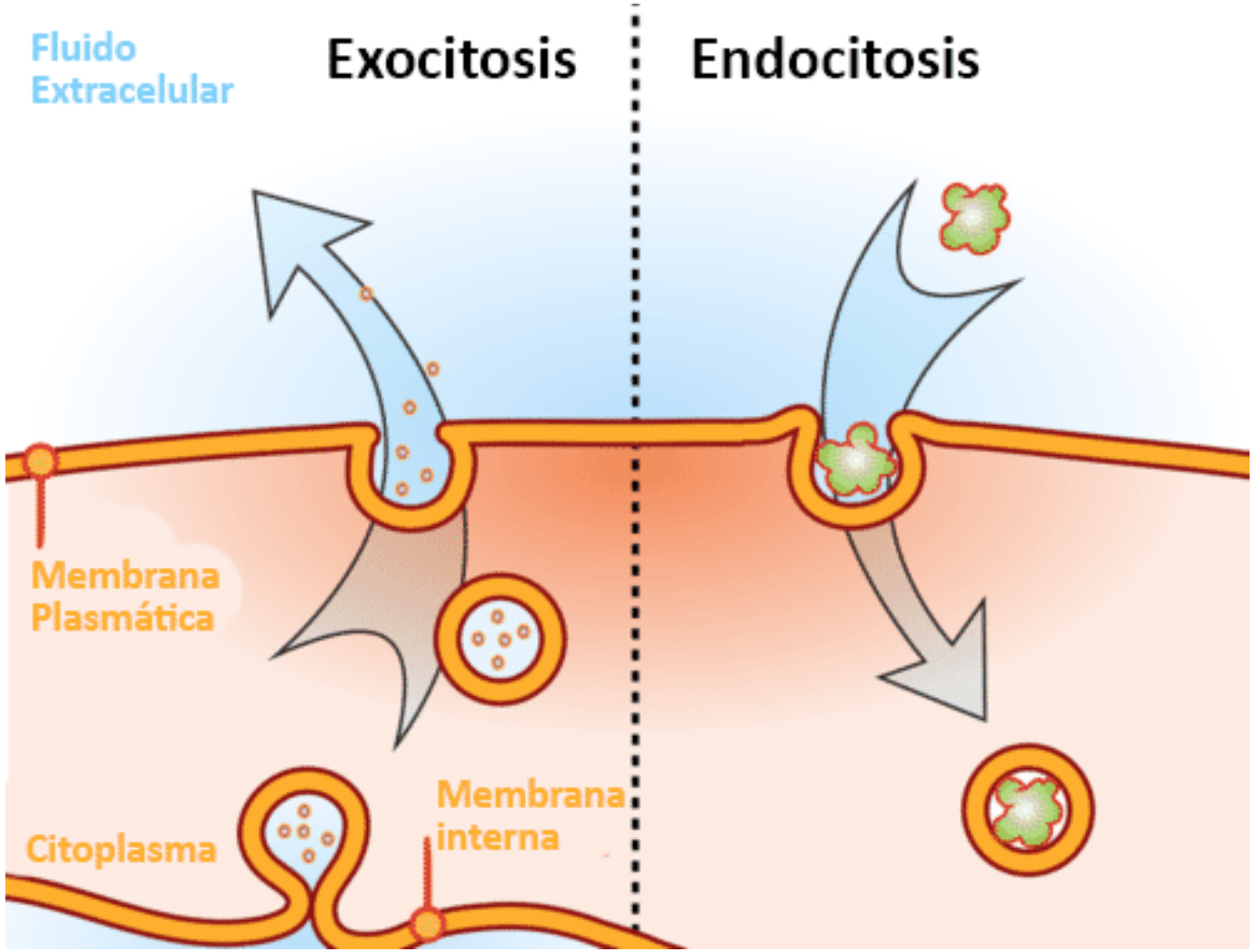
Transporte electrógeno

- Crea un potencial químico que además genera uno eléctrico



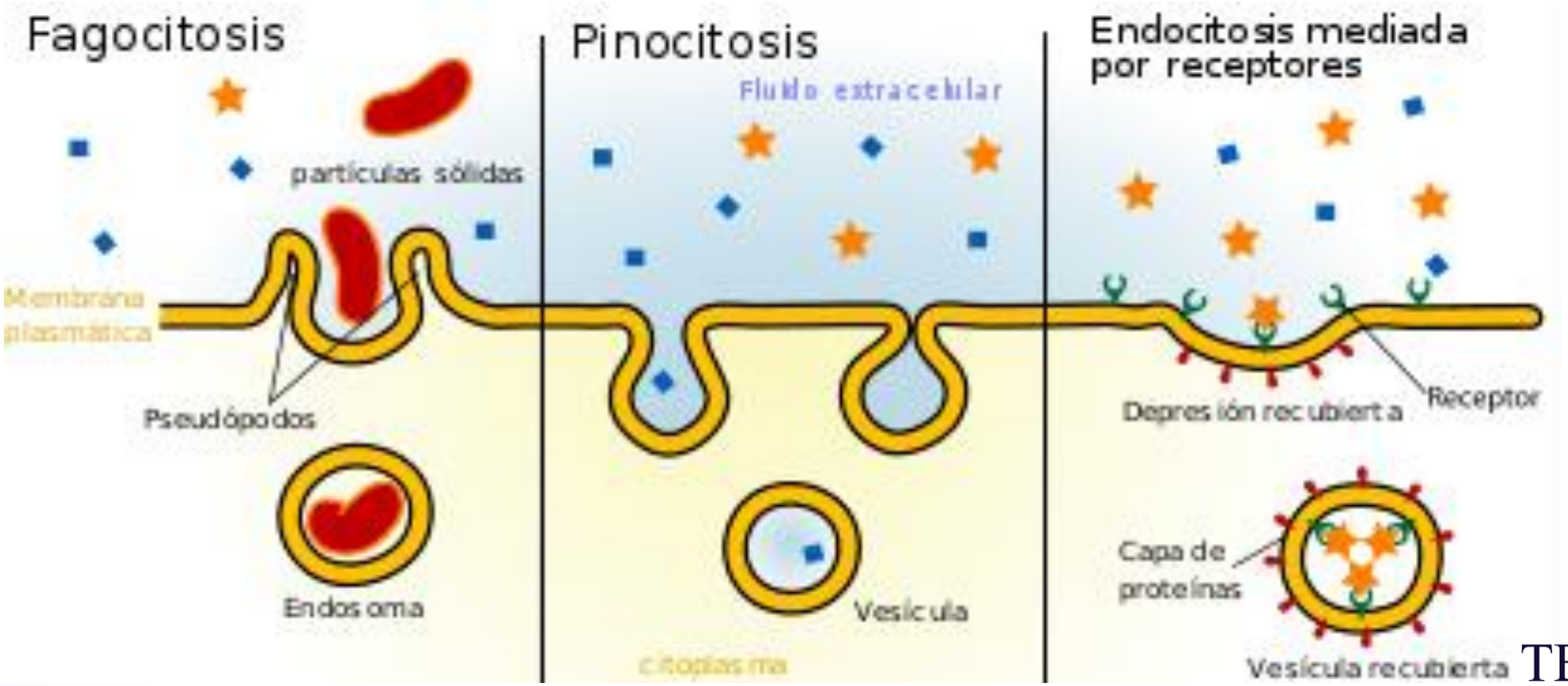

Espacio intermembranal
H+
H+
H+
H+
H+
H+
Cit c
I
Q
II
III
IV
FADH2
FAD
+2H+
NADH
NAD+ + H+
2H+ + 1/2O2
H2O
2e–
Matriz mitocondrial
Membrana mitocondrial interna

Endocitosis y Exocitosis



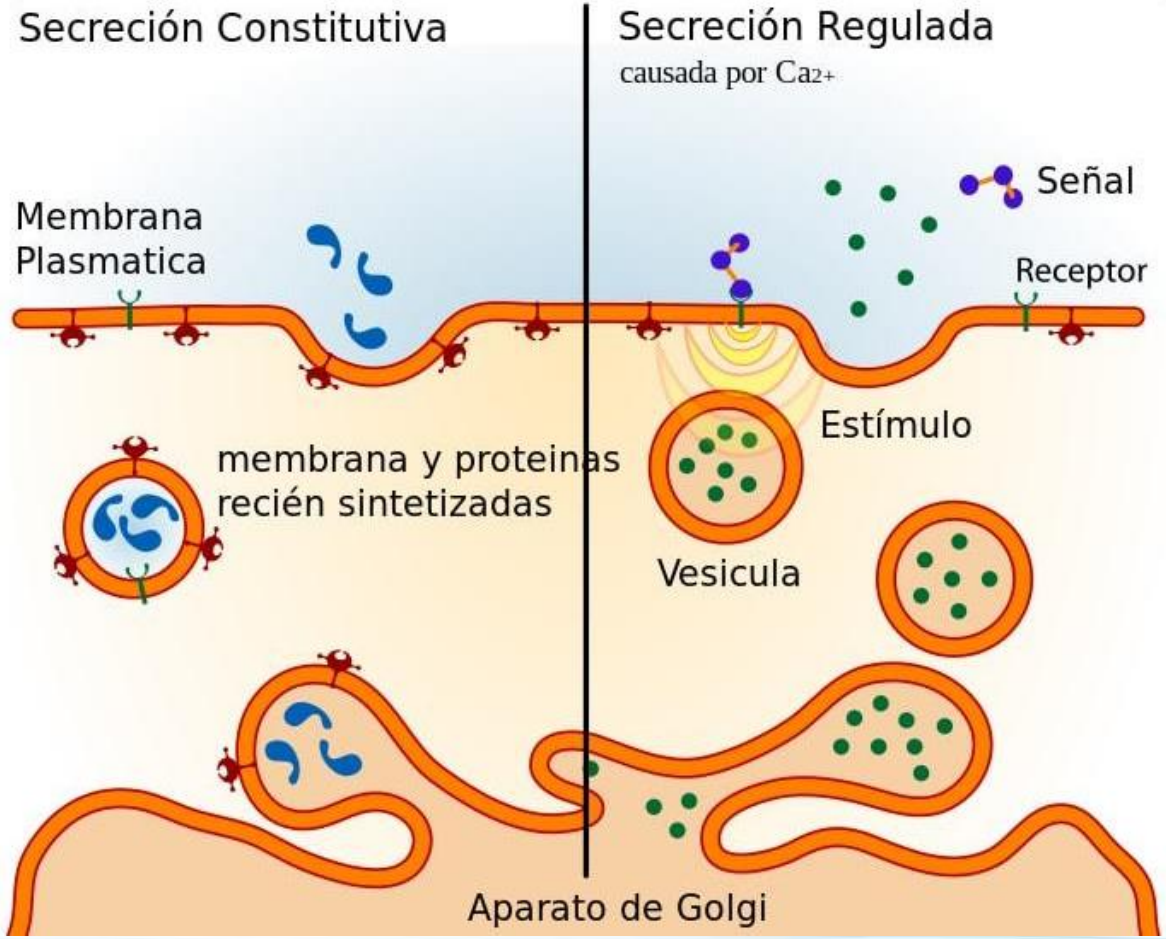
Endocitosis

- Inespecífica o constitutiva *vs*. Específica o mediada por receptor



Exocitosis

- Constitutiva vs. Regulada



Comunicación celular y transducción de señal

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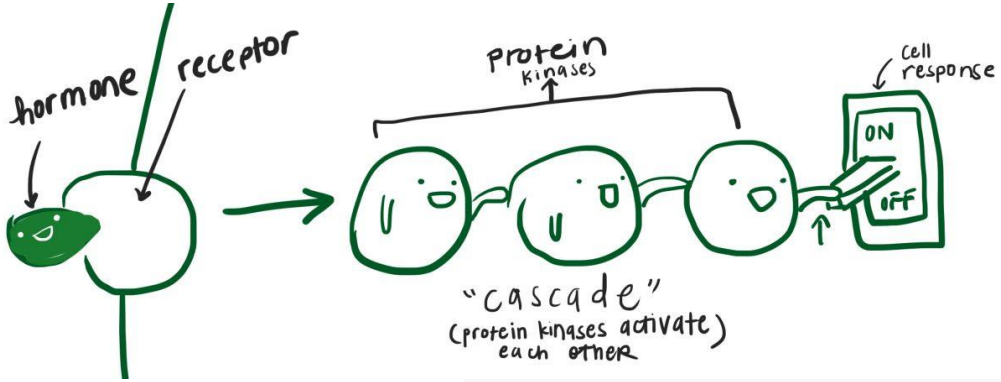
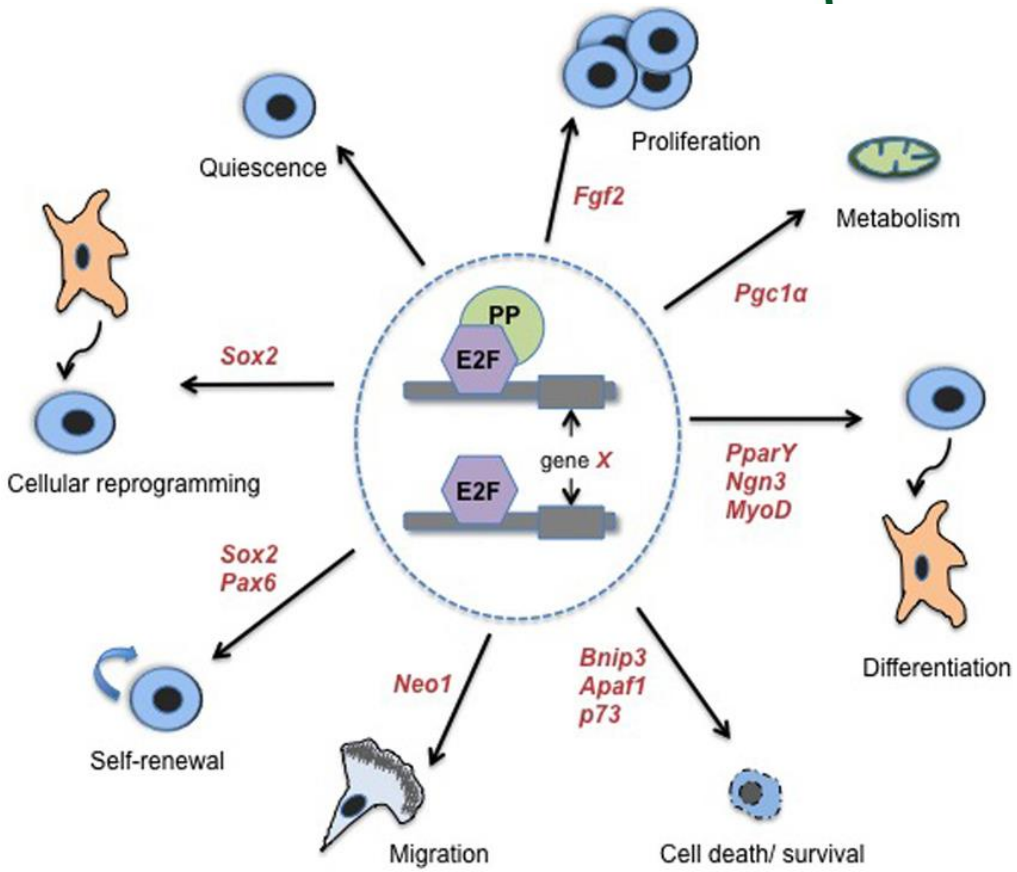
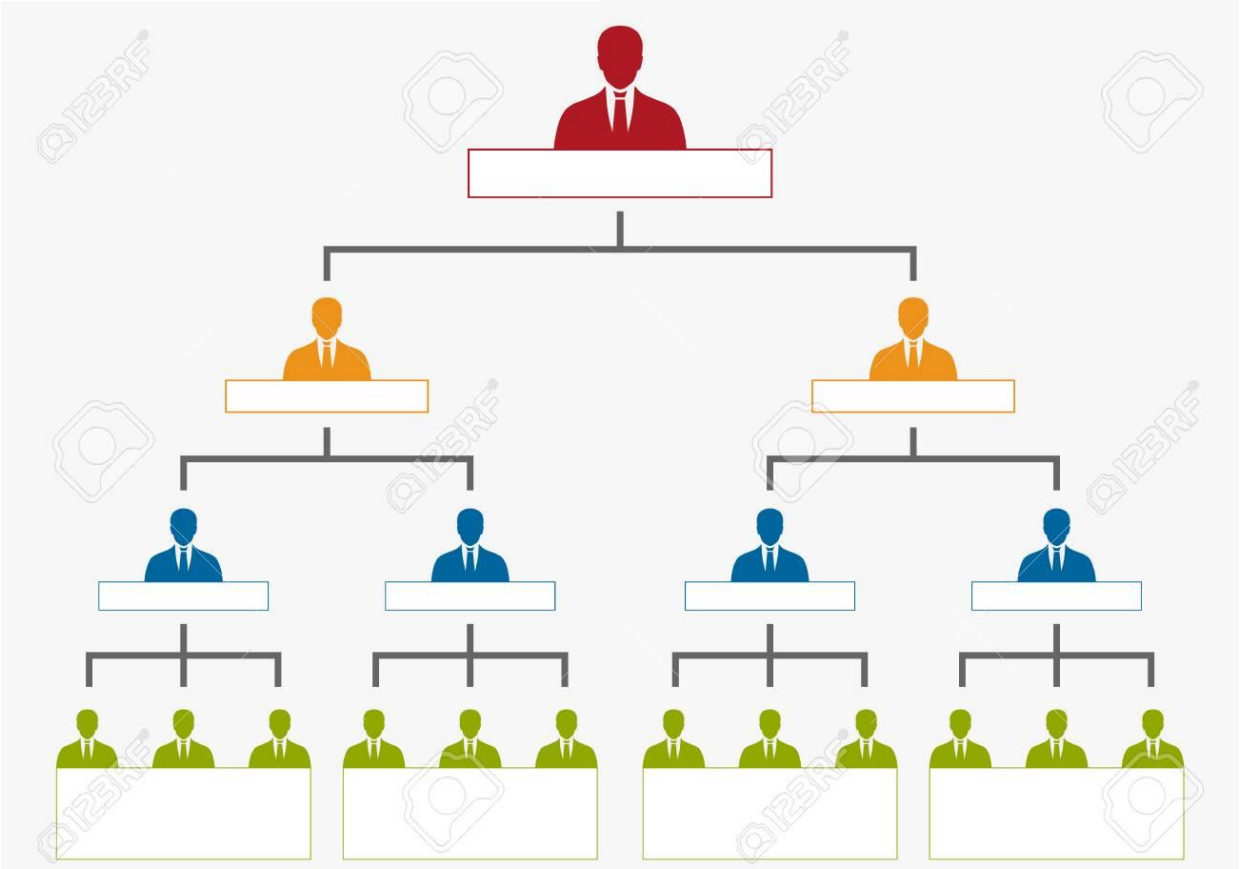
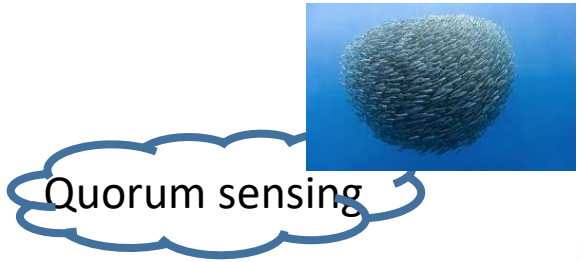

hormone
receptor
protein kinases
cell response
ON
OFF
"cascade"
(protein kinases activate each other)

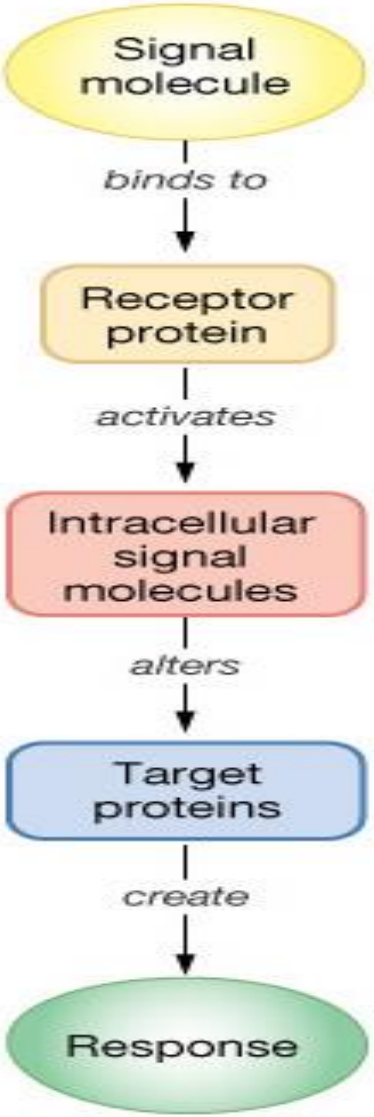

Quiescence
Proliferation
Fgf2
Metabolism
Pgc1α
PP
E2F
Sox2
Cellular reprogramming
gene X
E2F
PparY
Ngn3
MyoD
Differentiation
Sox2
Pax6
Self-renewal
Neo1
Migration
Bnip3
Apaf1
p73
Cell death/ survival



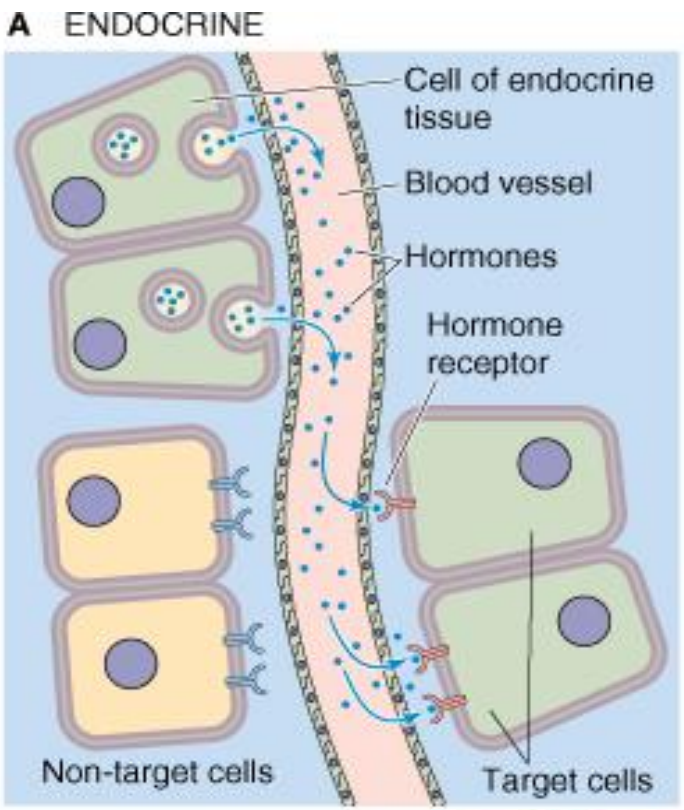
Comunicación celular

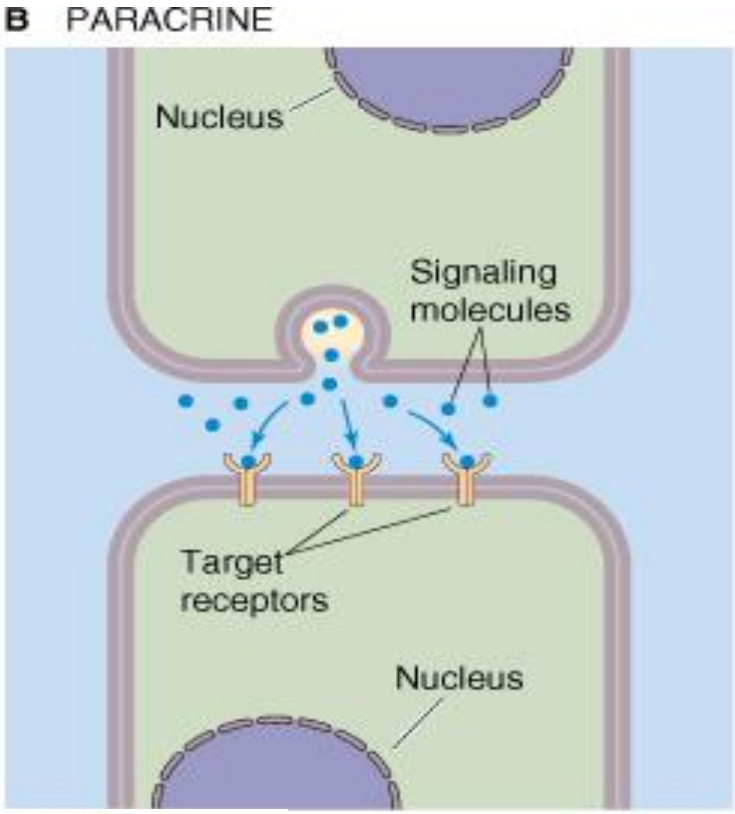
- Fundamental para todos los procesos biológicos
- Integra células vecinas o distantes
- Mecanismos:
  - Uniones estrechas
  - Comunicación yuxtacrina
  - Señales químicas
    - Autocrina, Paracrina, Endocrina
      - Aminas
      - Péptidos y proteínas
      - Esteroides
      - Moléculas pequeñas (AA, nts, iones)

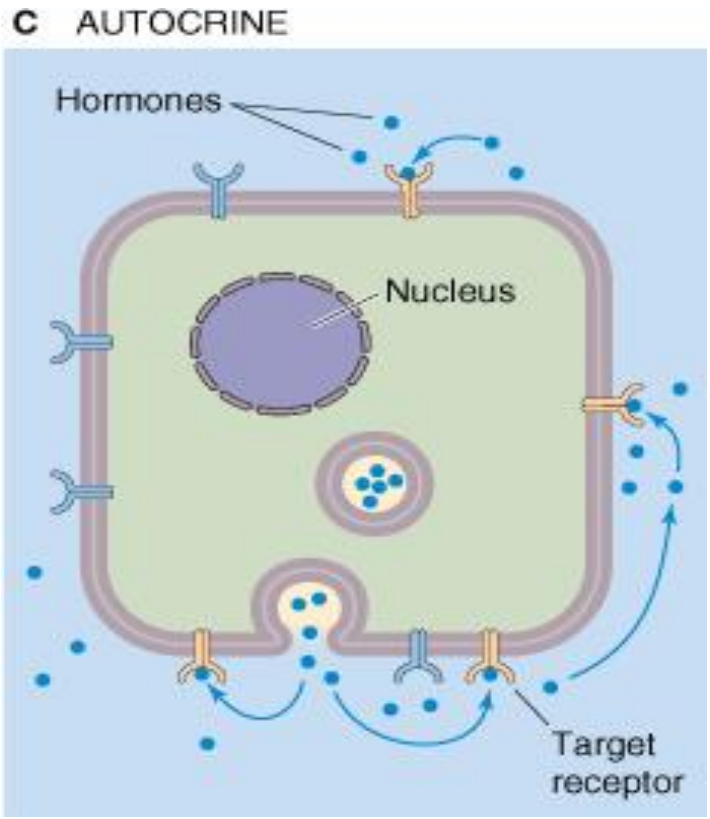


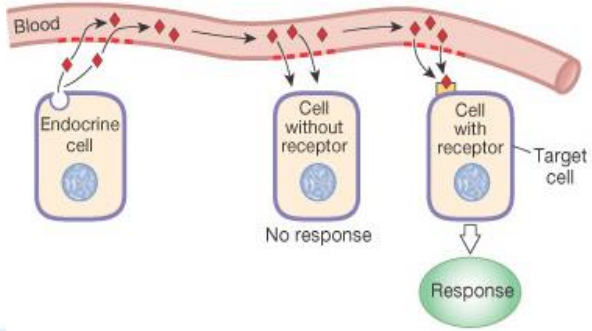


Señales químicas







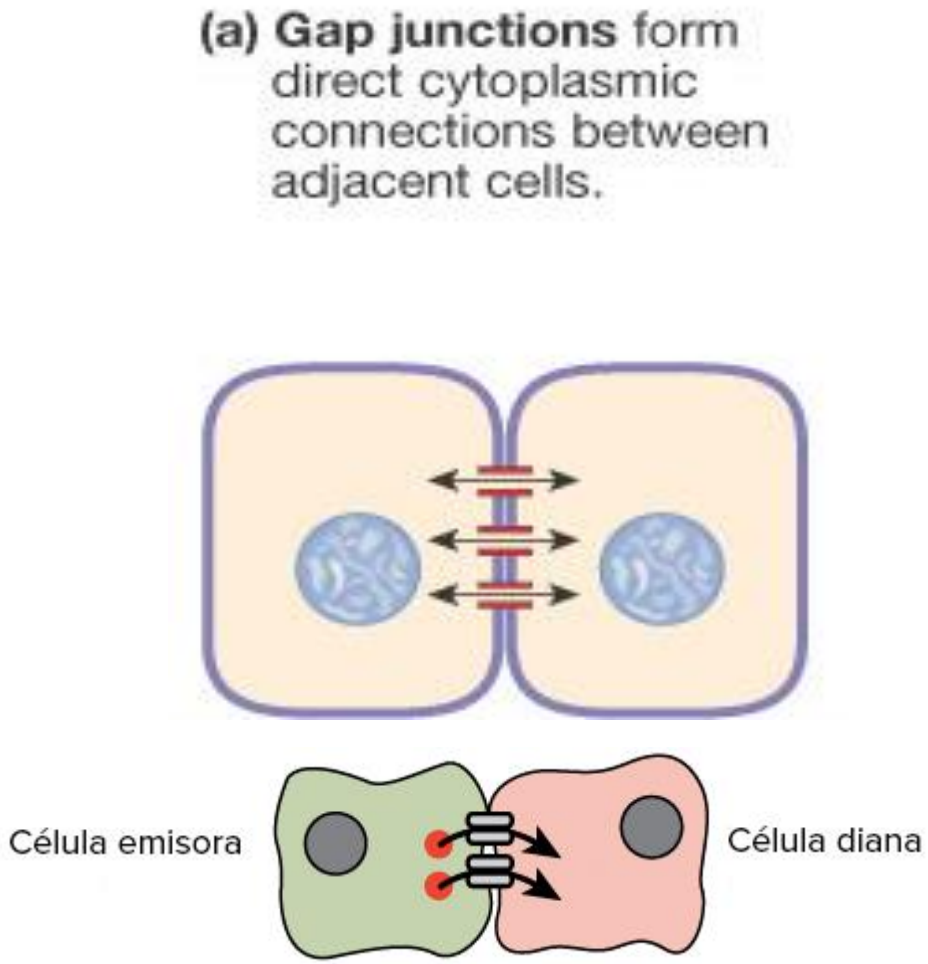


Gap junctions o uniones estrechas

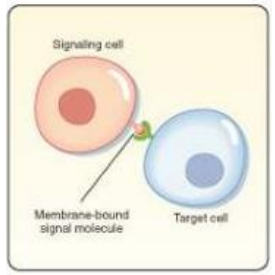
- Canales que permiten el paso de agua, iones, moléculas pequeñas y corriente eléctrica

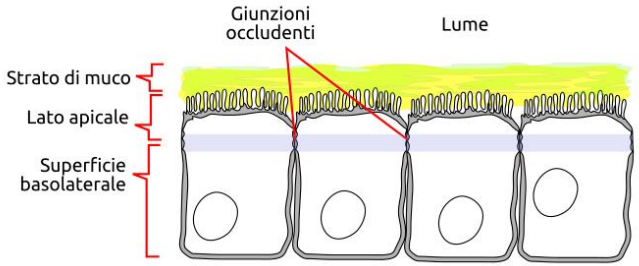
- Consisten en mitades de canales acoplados en células adyacentes

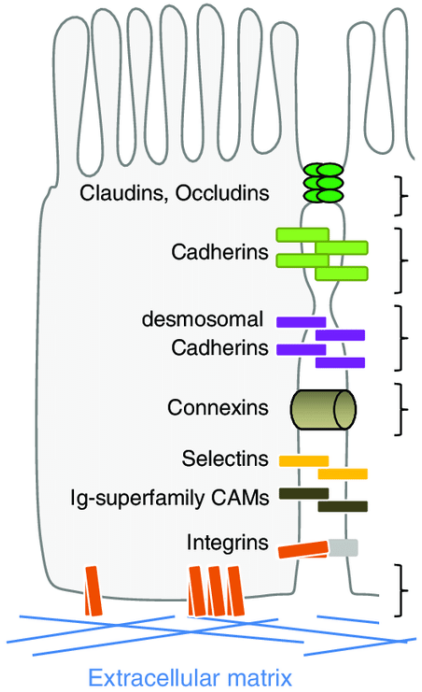
- Alternan entre estados abiertos o cerrados



Comunicación yuxtacrina







(1) Tight junction

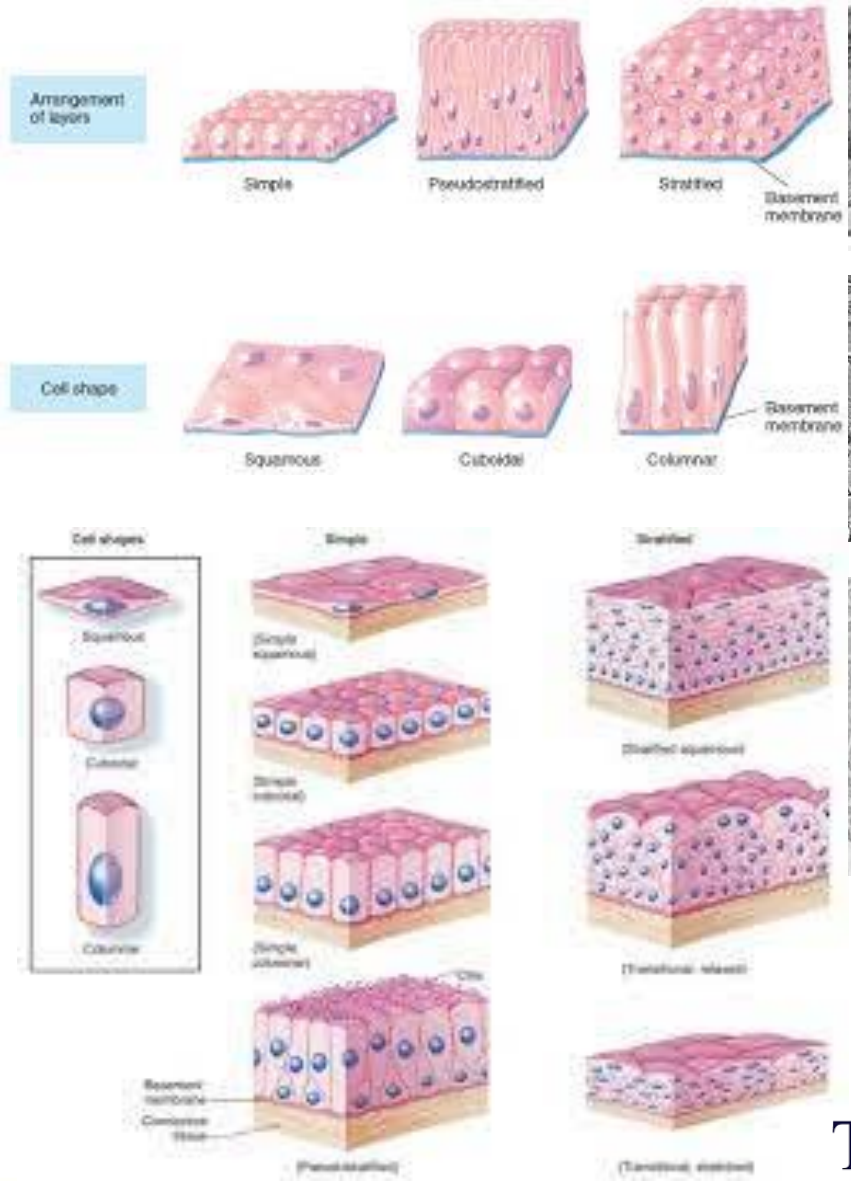
(2) Adherens junction

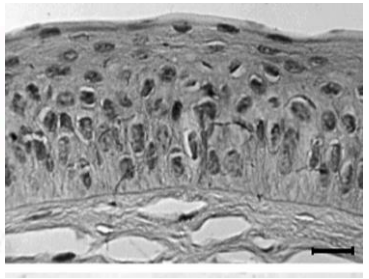
(3) Desmosome

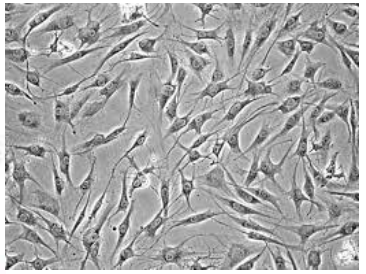
(4) Gap junction

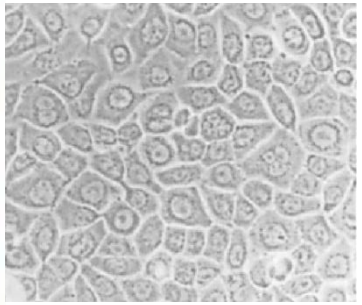
(5) Non-classical junctions

(6) Focal adhesion, Hemi-desmosome

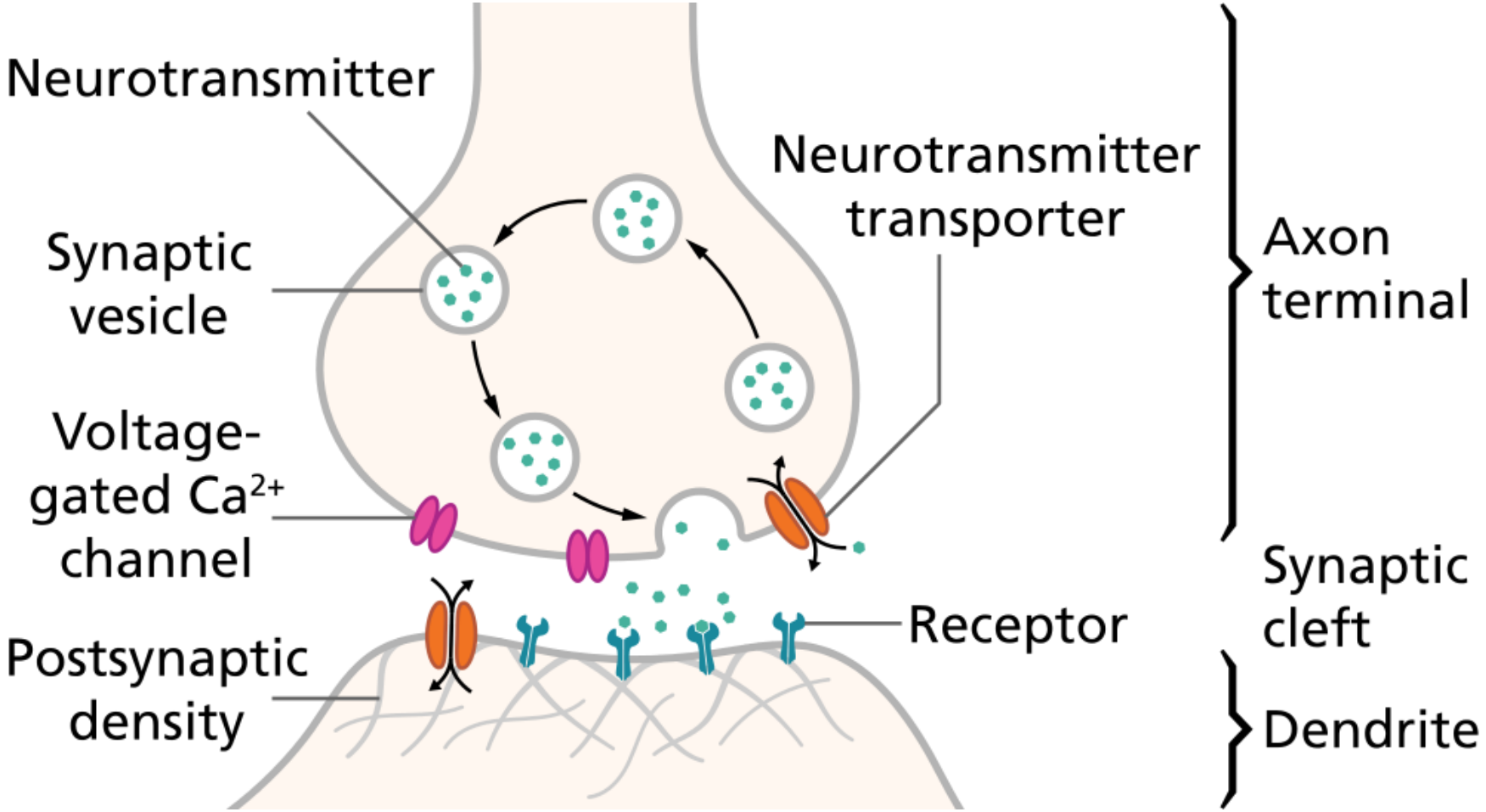






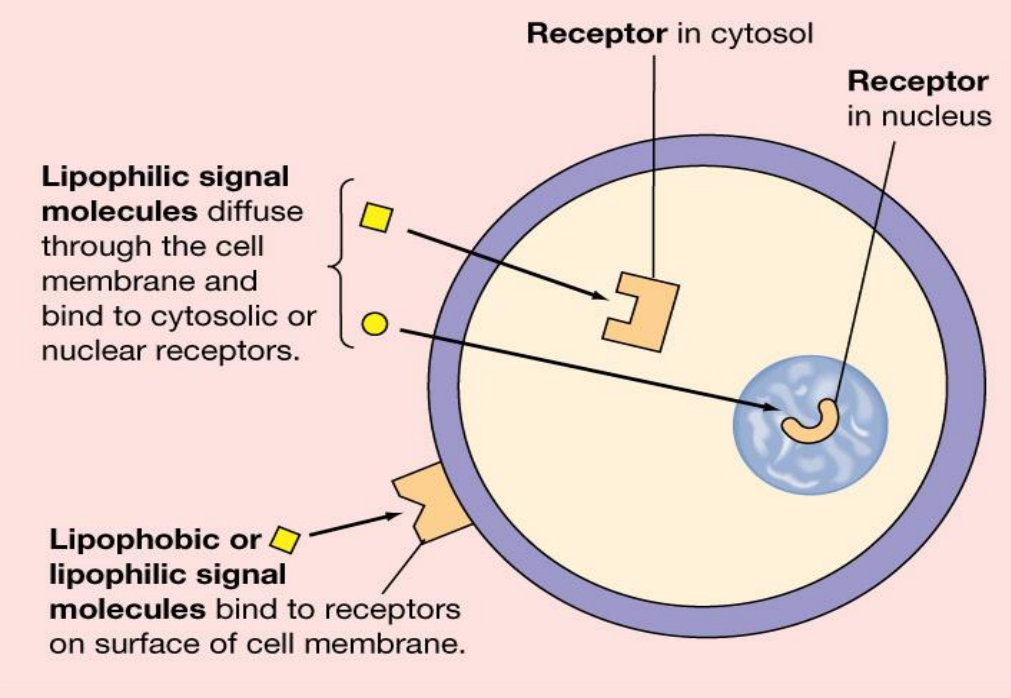


Combinación



Integración / Comunicación

- La “señal química” (ligando) interactúa con su blanco (célula) por unión a receptores superficiales (en la membrana) o intracelulares
- Ligando: Molécula que sirve como señal extracelular. Se une al receptor
- Receptor: Proteína en la superficie o dentro de la célula que une de manera específica al ligando
- El receptor puede ser un canal iónico pero por lo general la interacción ligando-receptor resulta en la asociación del receptor con un efector

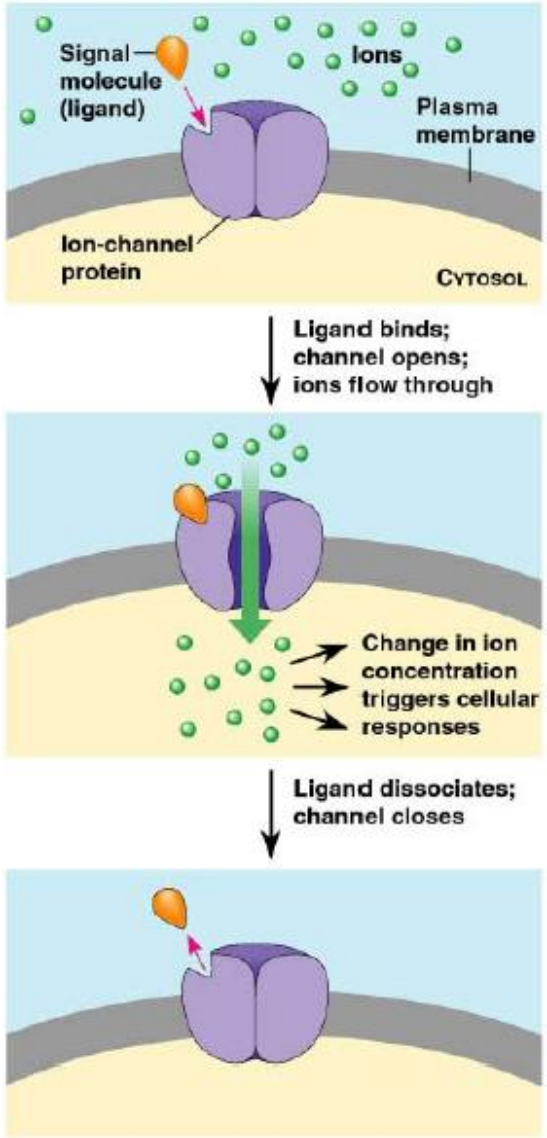


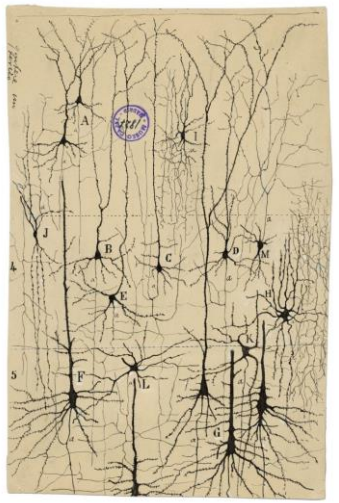
Tipos de receptor

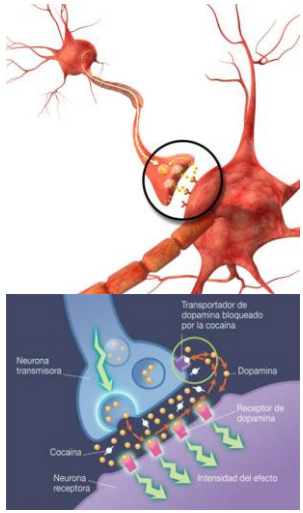
- Canales operados por ligando (receptores ionotrópicos o nicotínicos)
- Receptores acoplados a proteínas G (metabotrópicos o muscarínicos)
- Receptores catalíticos
- Receptores intracelulares
- Proteínas transmembrana que liberan factores de transcripción

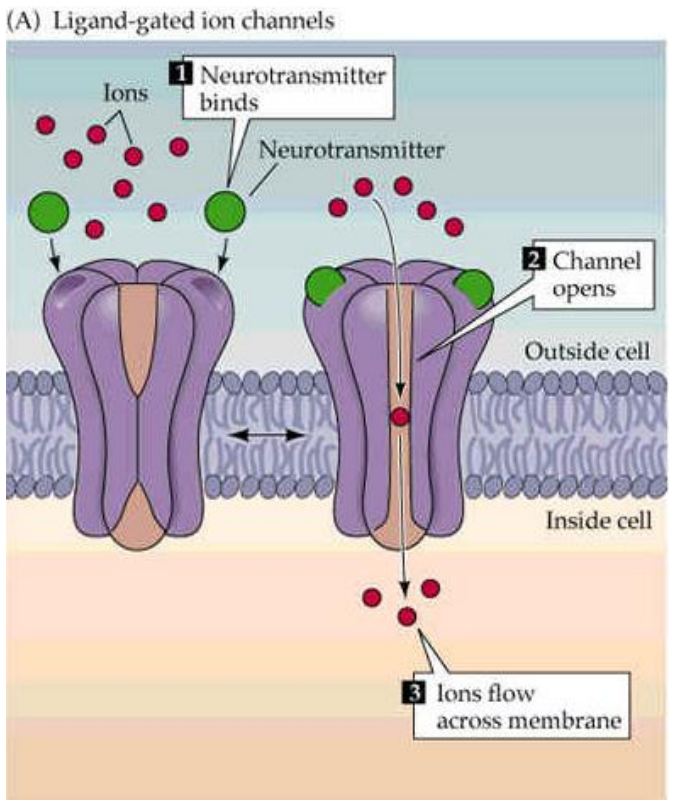
Canales operados por ligando o receptores ionotrópicos

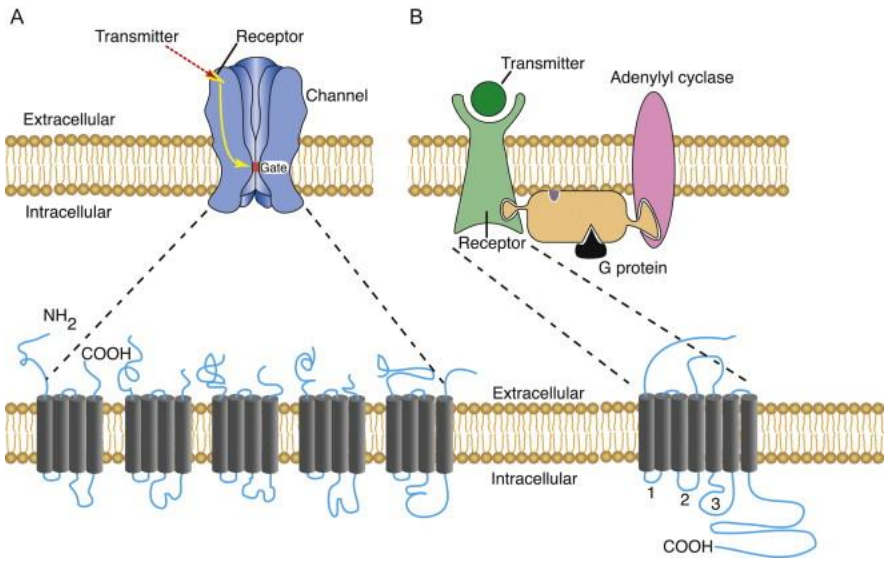
- Señalamiento entre células eléctricamente excitables
- La unión del neurotransmisor al receptor resulta en la apertura temporal del canal, alterando la permeabilidad de la célula a los iones
- Na^{+}, K^{+} y Ca^{2+}

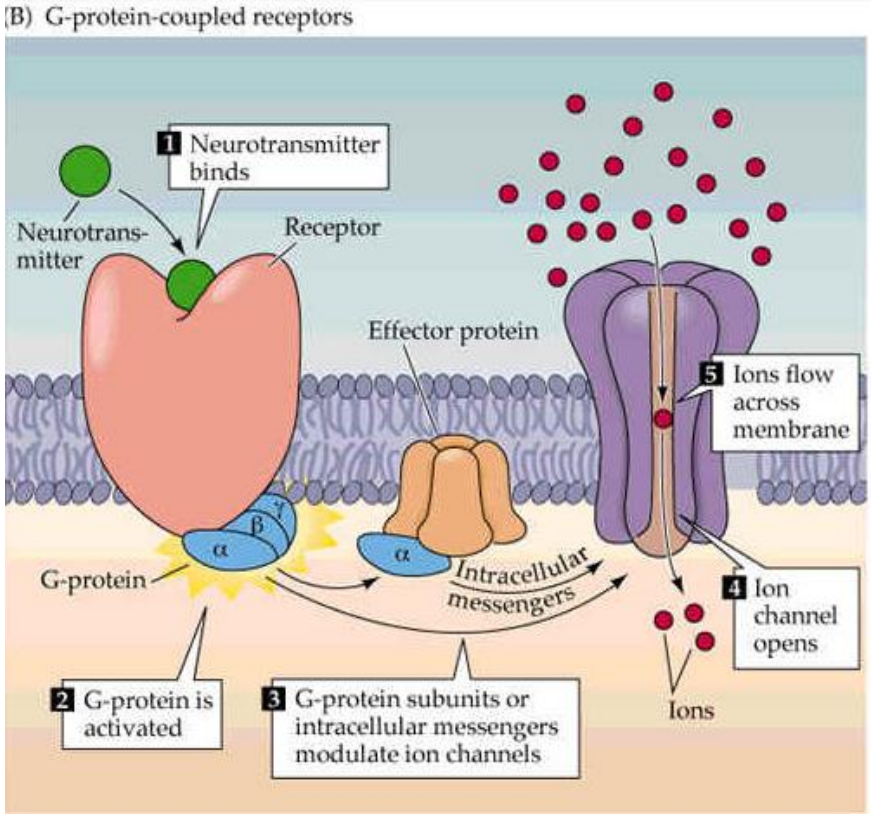










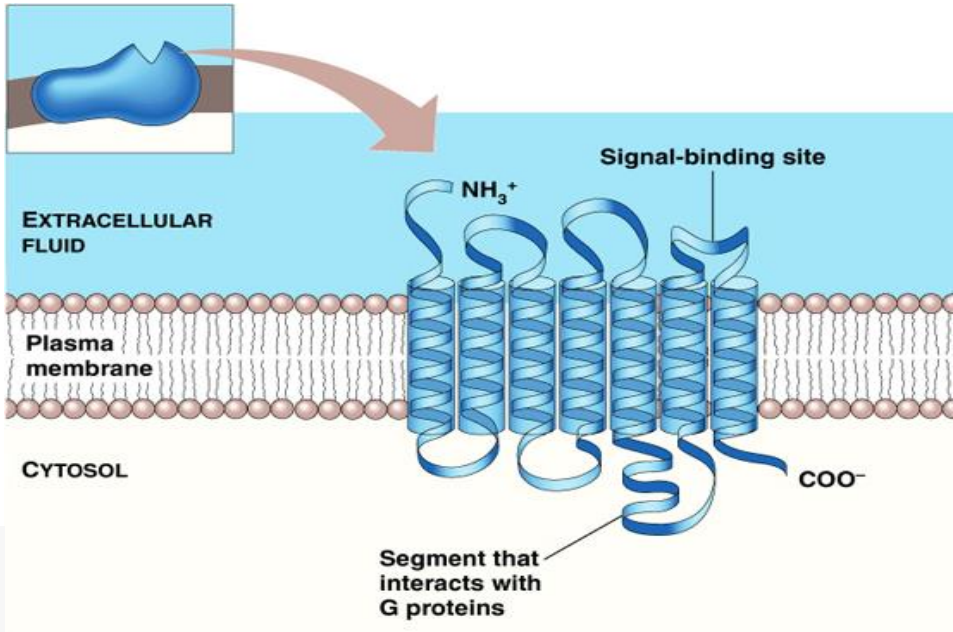


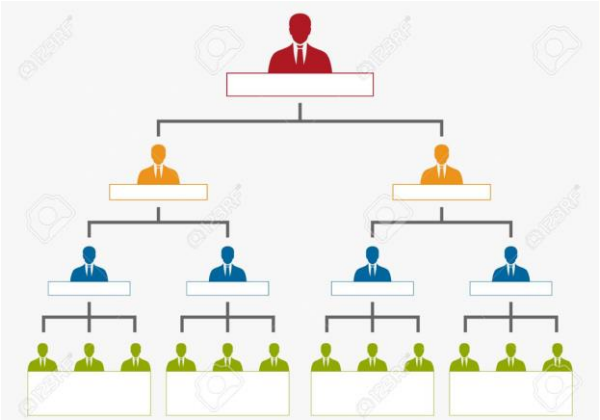
Activados por Ligando
Activados por fosforilación
Activados por voltaje
Activados mecánicamente (por estiramiento o presión)

Receptores acoplados a proteínas G

- Trabajan indirectamente (por un intermediario) para activar o inactivar canales o enzimas asociados a membrana

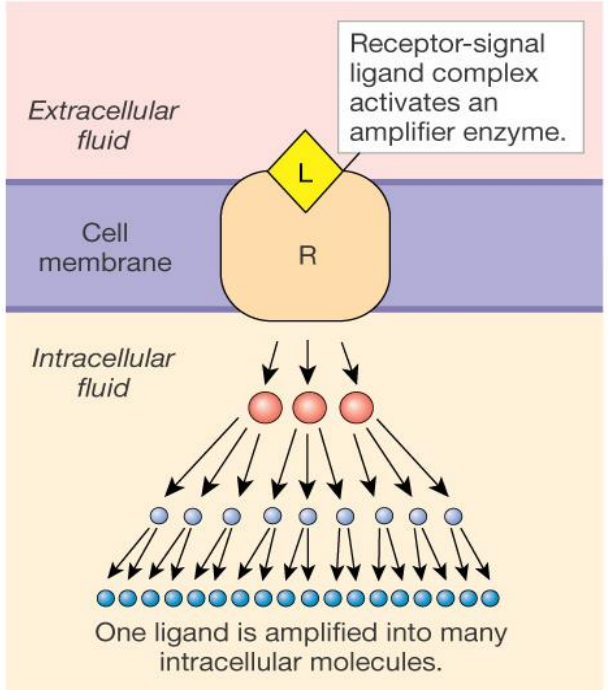
- El intermediario es un complejo unido a GTP (Proteína G)

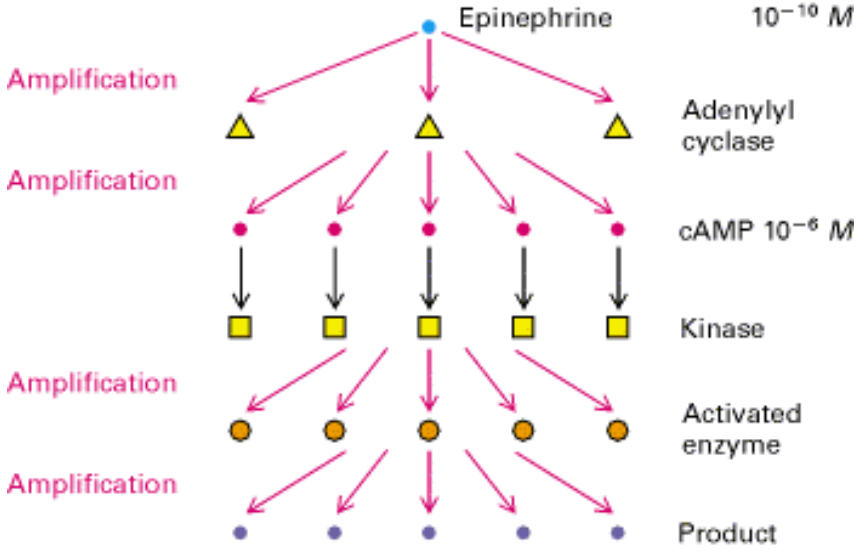




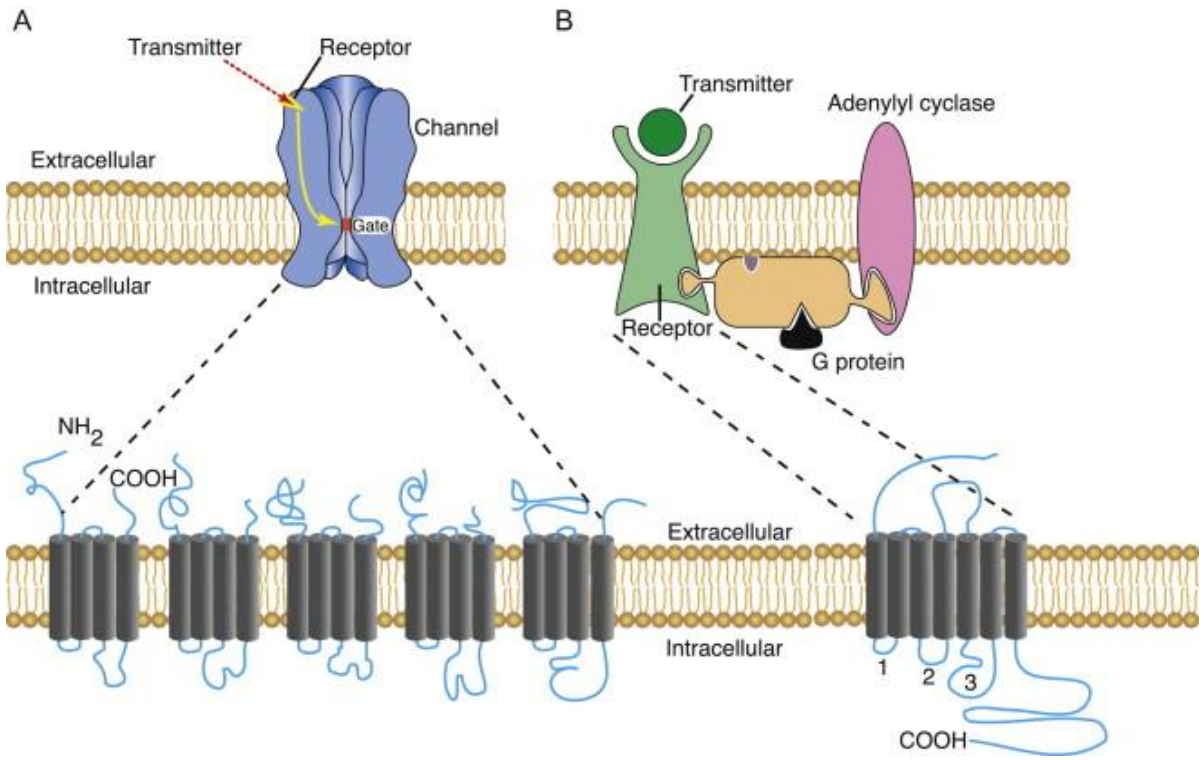
Segundos mensajeros

- Su concentración o actividad es finamente regulada
- Permiten amplificar la señal, especificidad y diversidad (diferentes ligandos en misma señal o mismo ligando en diferentes células)
- Principales ejemplos:
  - AMPc, GMPc, Inositol trifosfato, diacilglicerol, calcio, etc





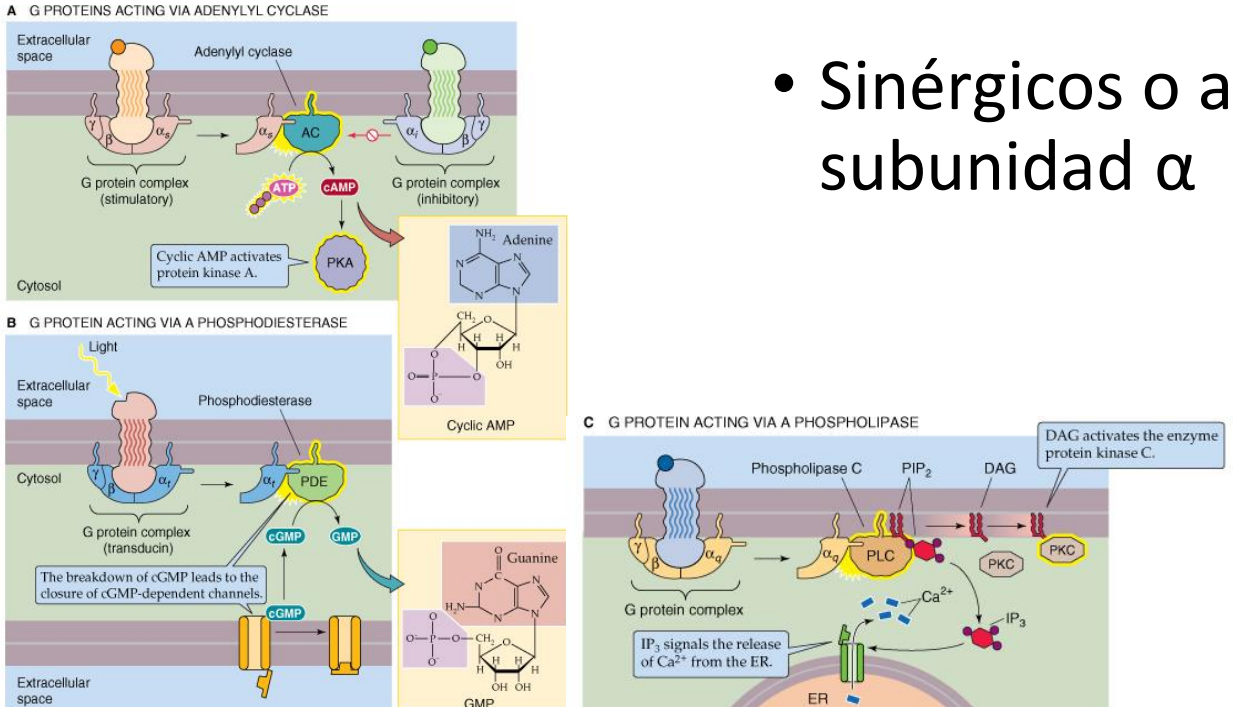
- Familia de la rodopsina o «Clase A»
  - Grupo α: receptores aminérgicos
    - Receptores adrenérgicos.
    - Receptores muscarínicos.
    - Receptores dopaminérgicos.
    - Receptores histaminérgicos.
    - Receptores serotoninérgicos.
    - Receptores de trazas de aminas.
  - Grupo β.
  - Grupo γ.
  - Grupo δ.
  - Grupo κ.
  - Grupo μ.



- Familia de la secretina o «Clase B»
- Familia de los receptores metabotrópicos de glutamato o «Clase C»
- Receptores de feromonas fúngicas o «Clase D», no presentes en vertebrados
- Receptores de AMP cíclico o «Clase E»
- Familia atípica de Frizzled o «Clase F»
- Familia adhesión

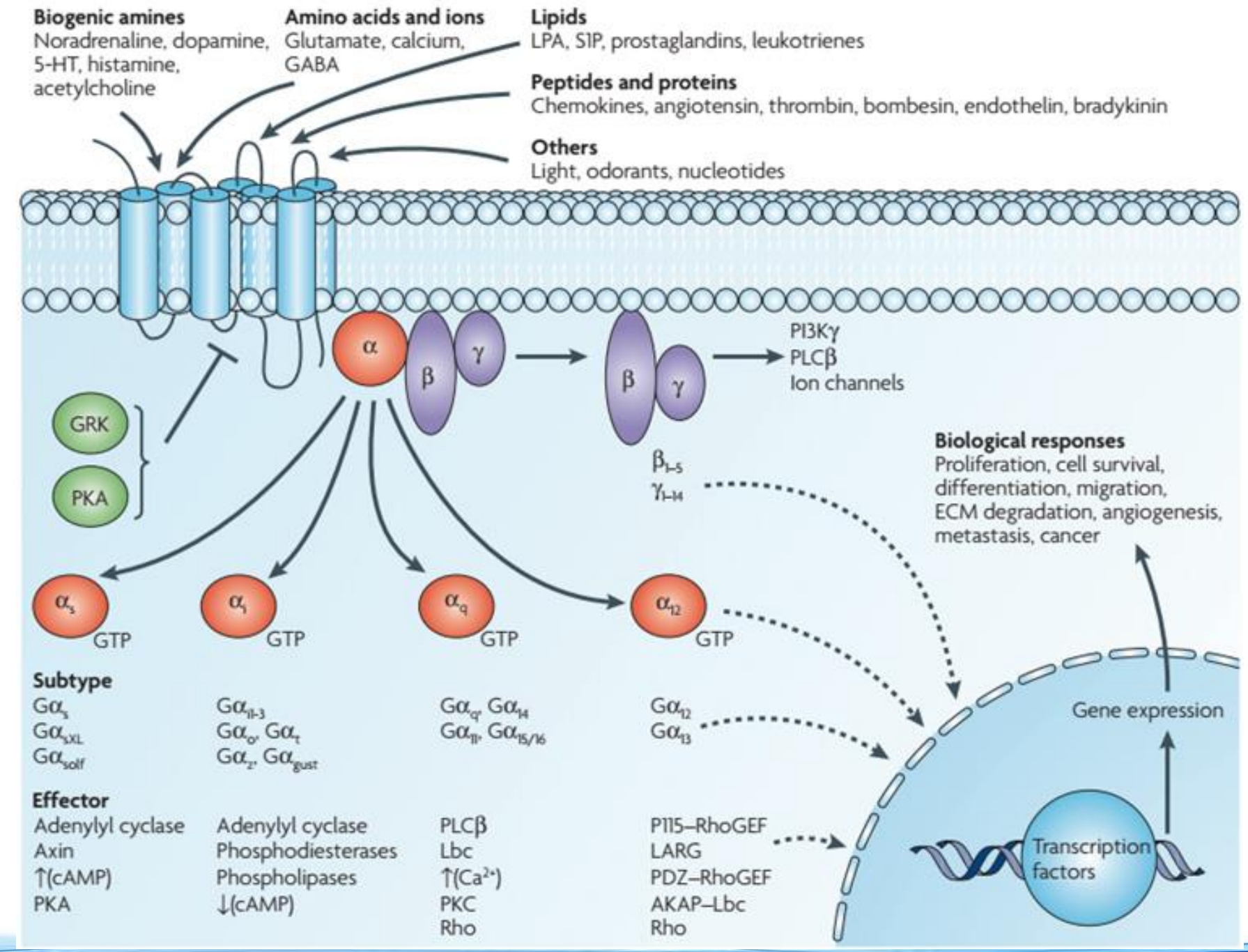
Efectores a los que se acopla la subunidad α activa

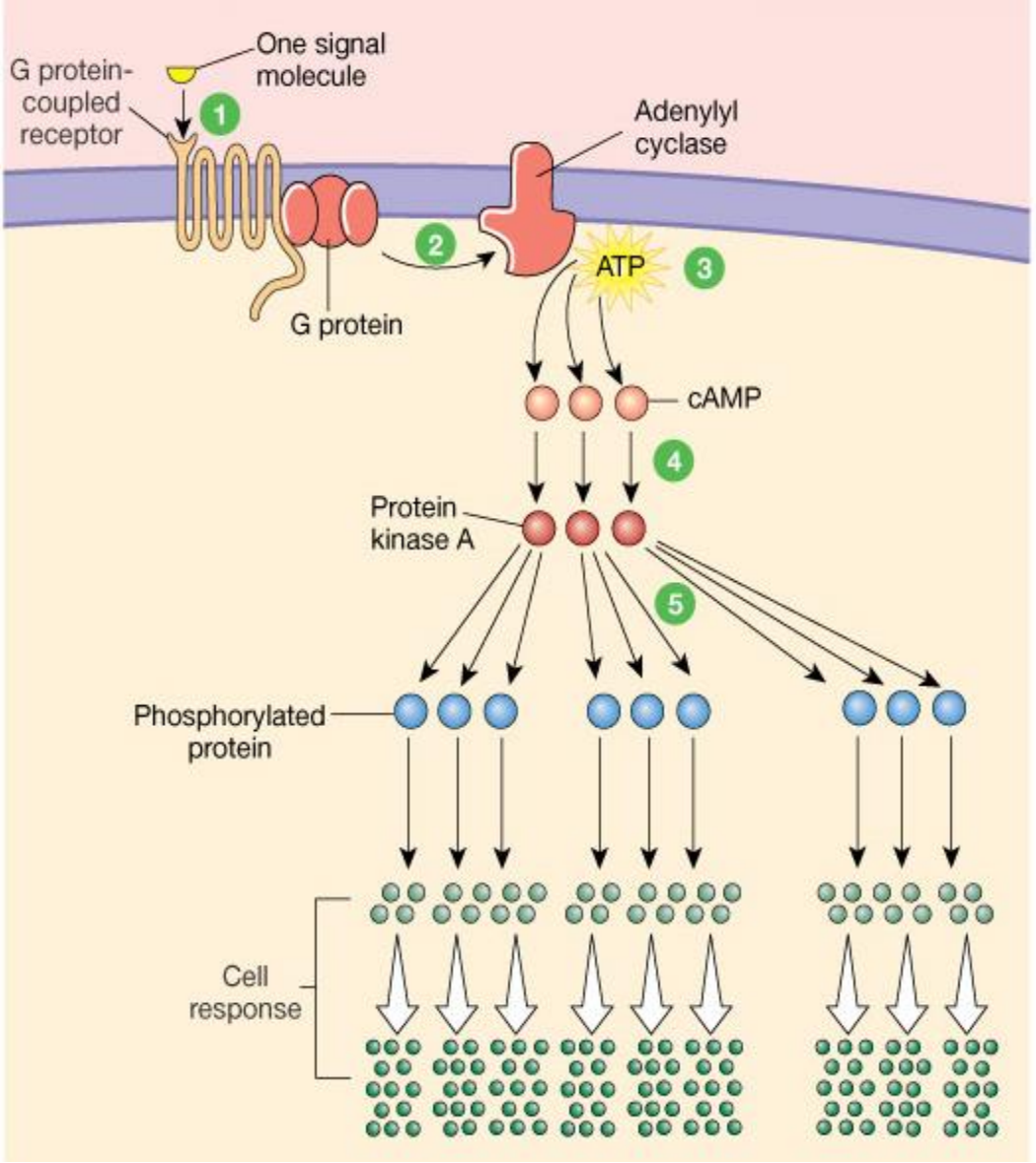
- Adenilato ciclasa
- Fosfodiesterasa
- Fosfolipasas
  - A2, C, D
- Canales iónicos



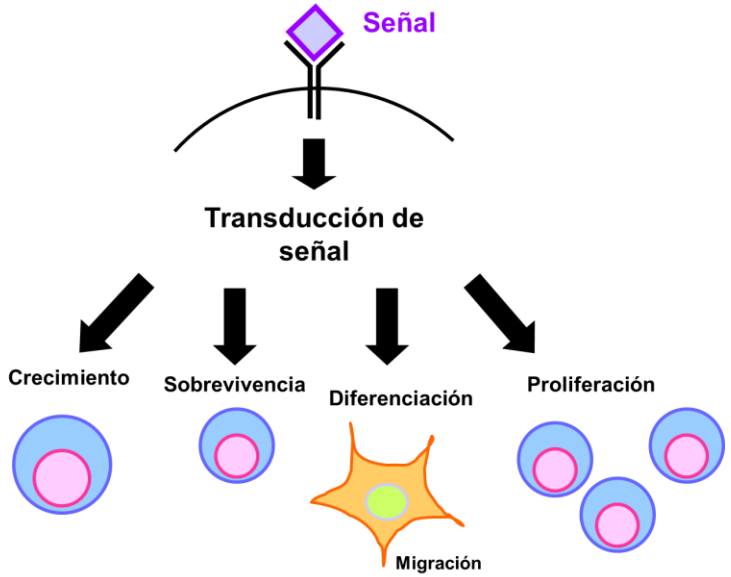
Efectores a los que se acopla el complejo βγ

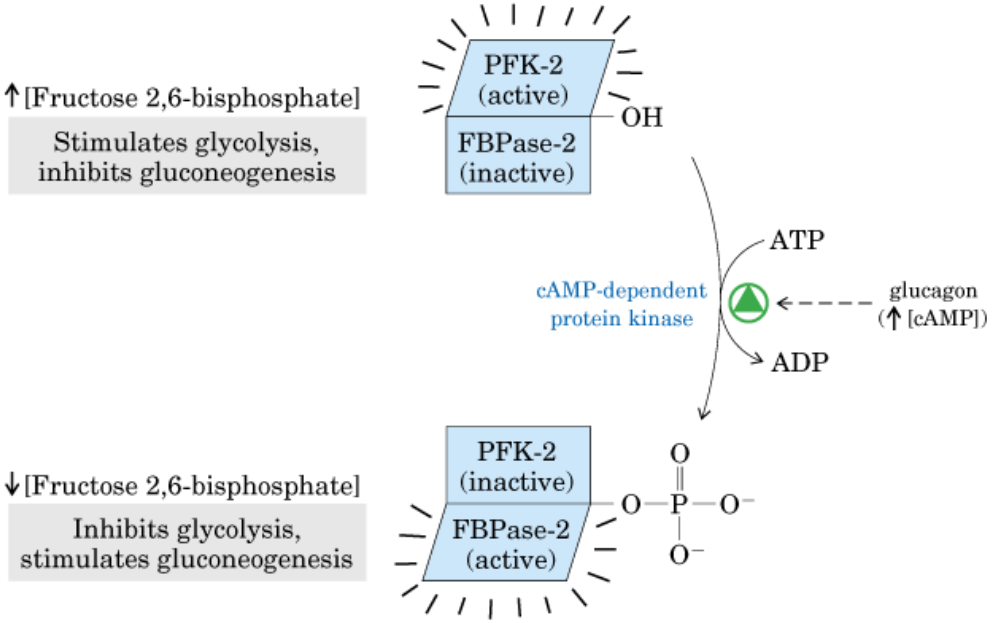
- Adenilato ciclasa
- Fosfolipasa C
- Canales iónicos
- Sinérgicos o antagonistas de la subunidad α

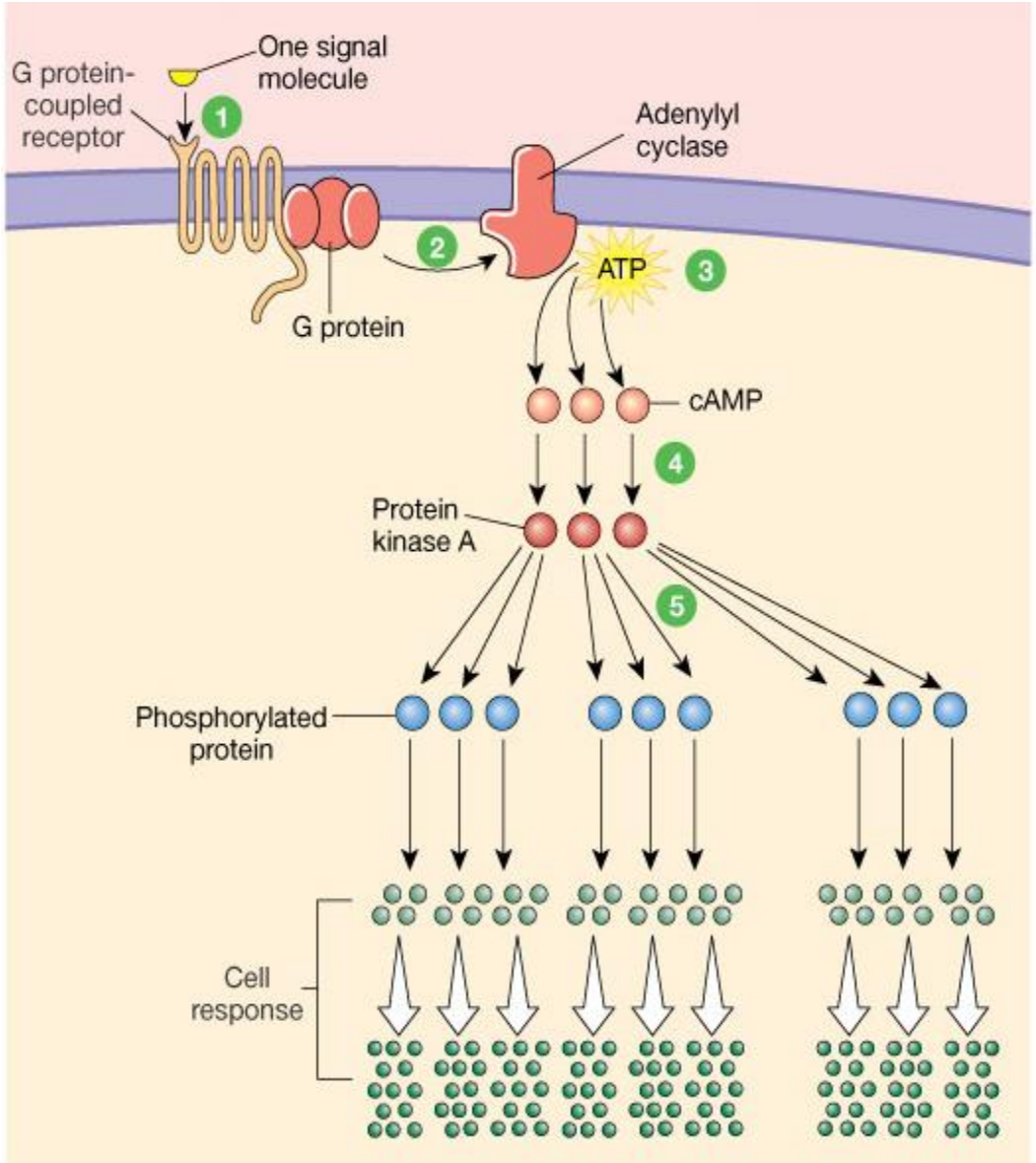

Biogenic amines
Noradrenaline, dopamine, 5-HT, histamine, acetylcholine
Amino acids and ions
Glutamate, calcium, GABA
Lipids
LPA, S1P, prostaglandins, leukotrienes
Peptides and proteins
Chemokines, angiotensin, thrombin, bombesin, endothelin, bradykinin
Others
Light, odorants, nucleotides
α
β
γ
PI3Kγ
PLCβ
Ion channels
GRK
PKA
β_{1-5}
γ_{1-14}
Biological responses
Proliferation, cell survival, differentiation, migration, ECM degradation, angiogenesis, metastasis, cancer
α_s
α_i
α_q
α_{12}
GTP
Subtype
$G\alpha_s$
$G\alpha_{sXL}$
$G\alpha_{solf}$
$G\alpha_{i1-3}$
$G\alpha_o$, $G\alpha_t$
$G\alpha_z$, $G\alpha_{gust}$
$G\alpha_q$, $G\alpha_{14}$
$G\alpha_{11}$, $G\alpha_{15/16}$
$G\alpha_{12}$
$G\alpha_{13}$
Gene expression
Effector
Adenylyl cyclase
Axin
↑(cAMP)
PKA
Adenylyl cyclase
Phosphodiesterases
Phospholipases
↓(cAMP)
PLCβ
Lbc
↑(Ca^{2+})
PKC
Rho
P115–RhoGEF
LARG
PDZ–RhoGEF
AKAP–Lbc
Rho
Transcription factors



1. Signal molecule binds to G protein-linked receptor, which activates the G protein.
2. G protein turns on adenylyl cyclase, an amplifier enzyme.
3. Adenylyl cyclase converts ATP to cyclic AMP.
4. cAMP activates protein kinase A.
5. Protein kinase A phosphorylates other proteins, leading ultimately to a cellular response.







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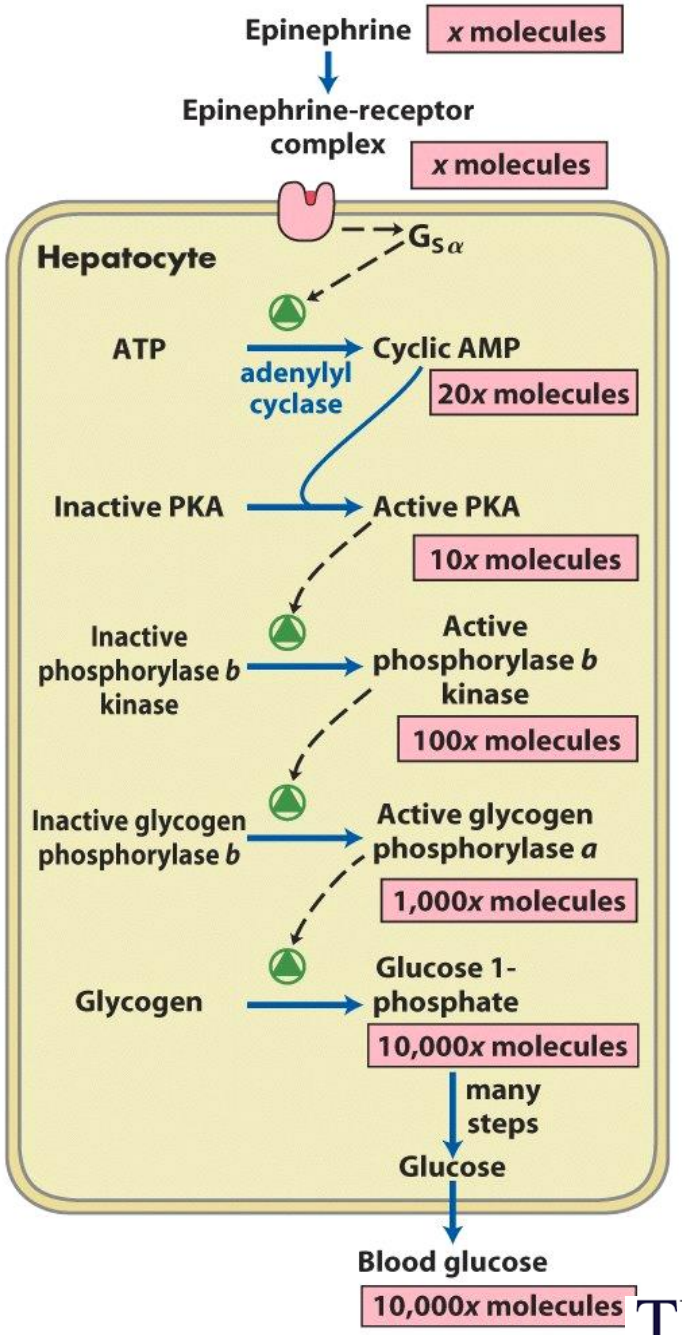
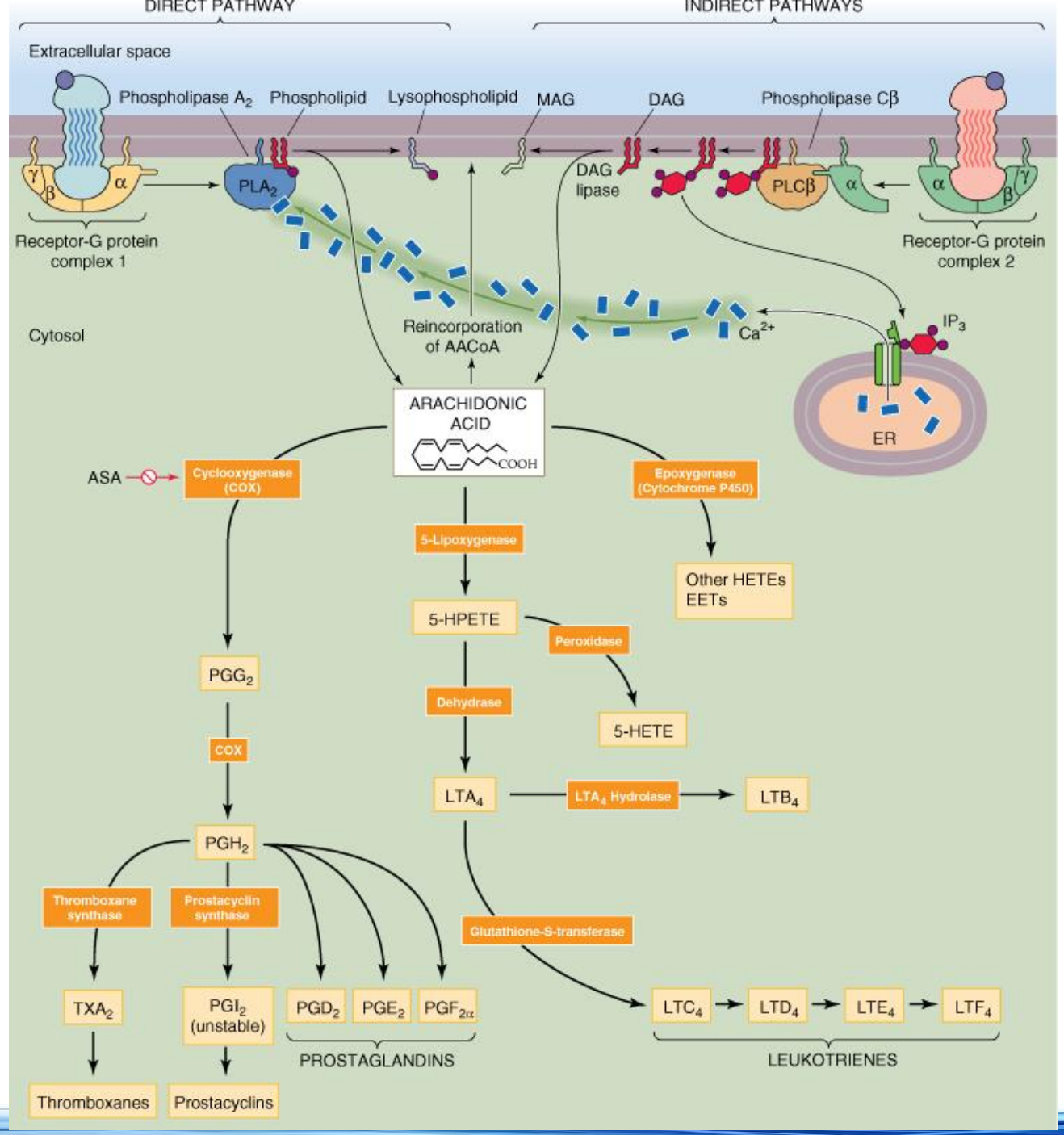


Metabolitos del ácido araquidónico

PLC y PLD pueden liberar DAG a partir de FC



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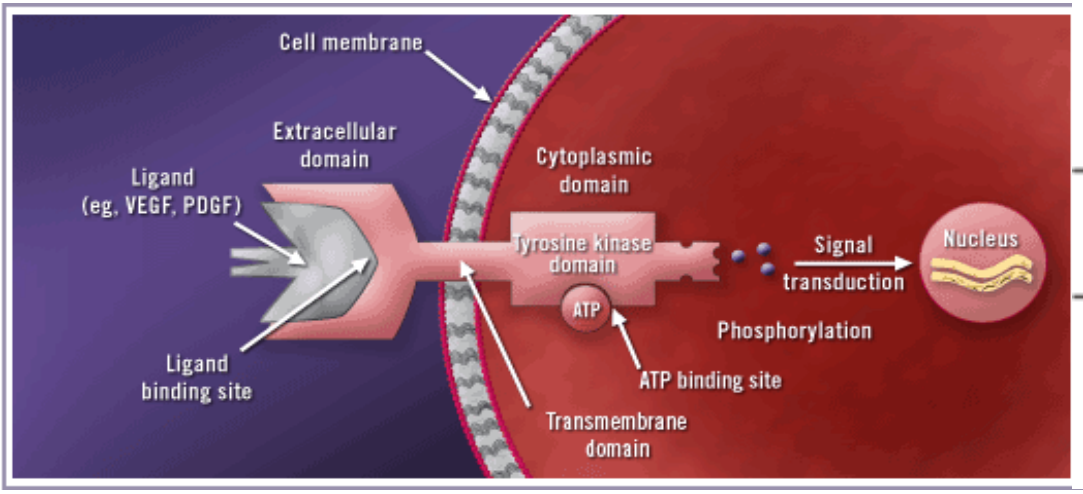
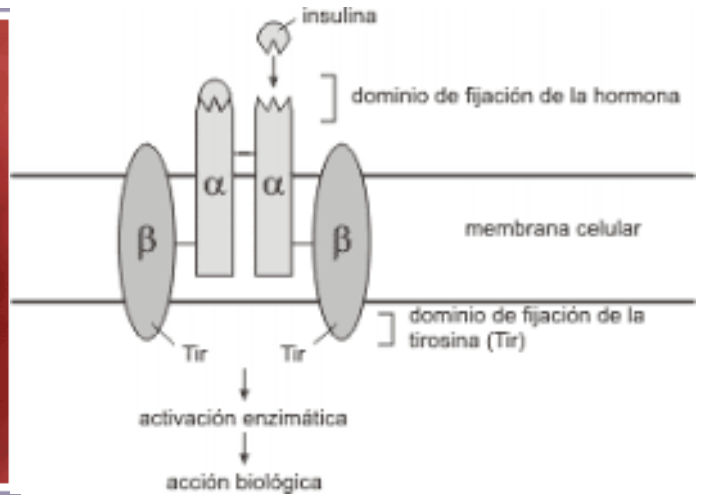
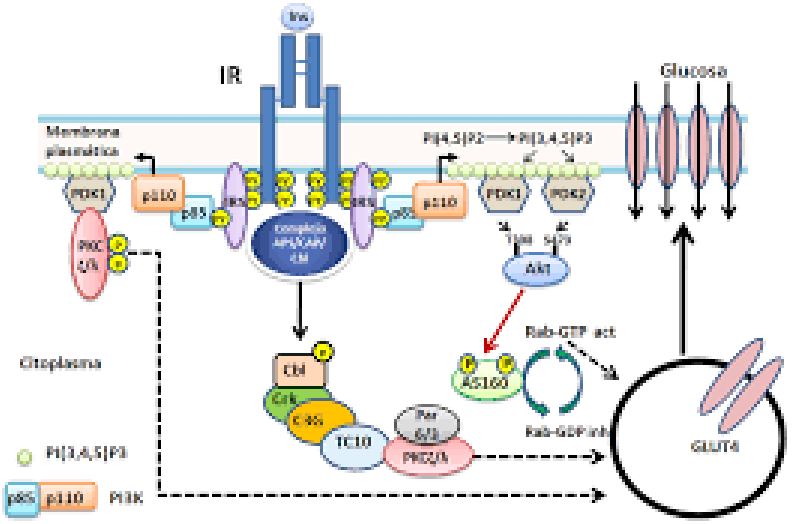
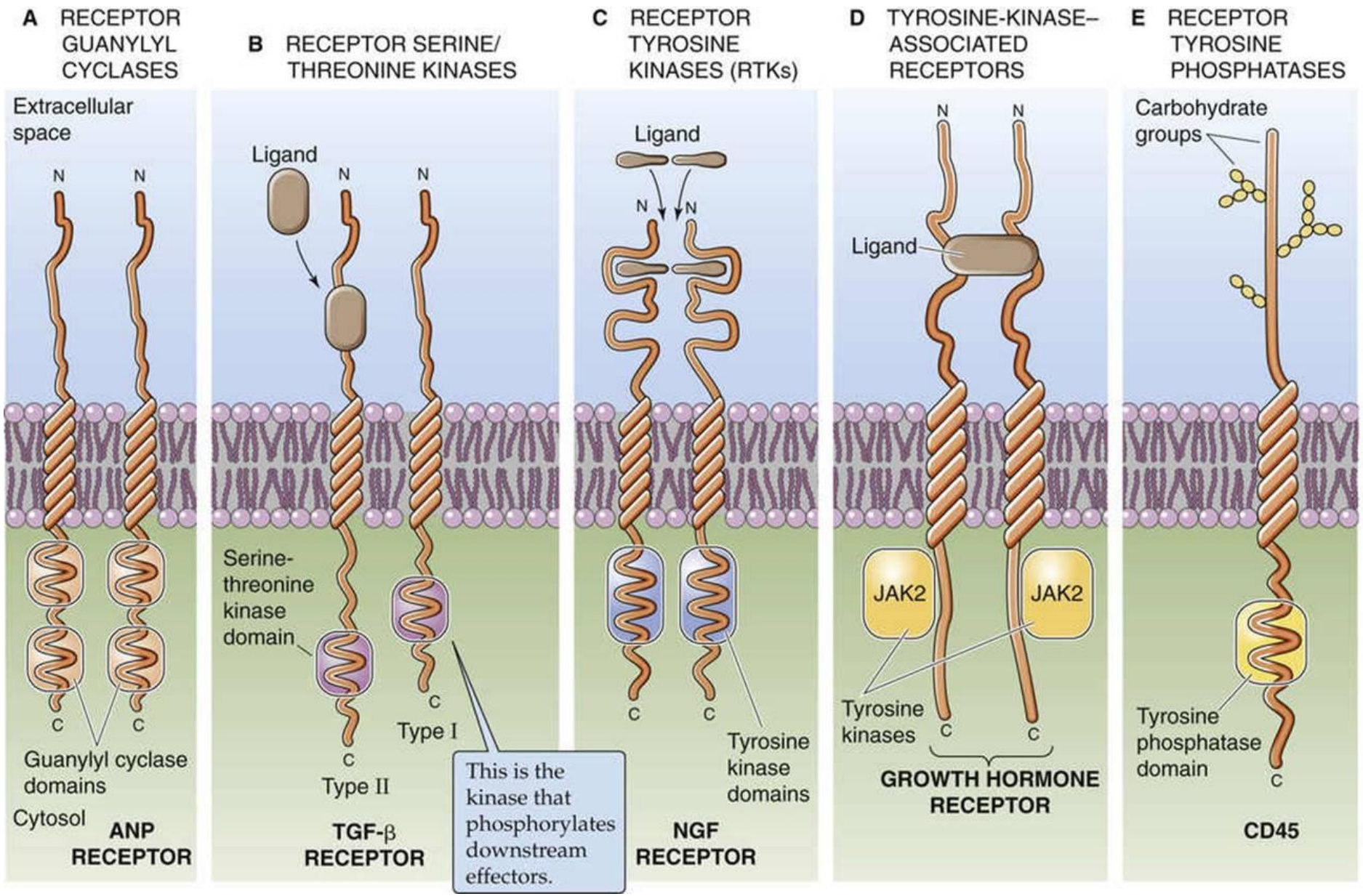
Receptores catalíticos

- Al activarse por el ligando ellos mismos funcionan como enzimas o como parte de complejos enzimáticos



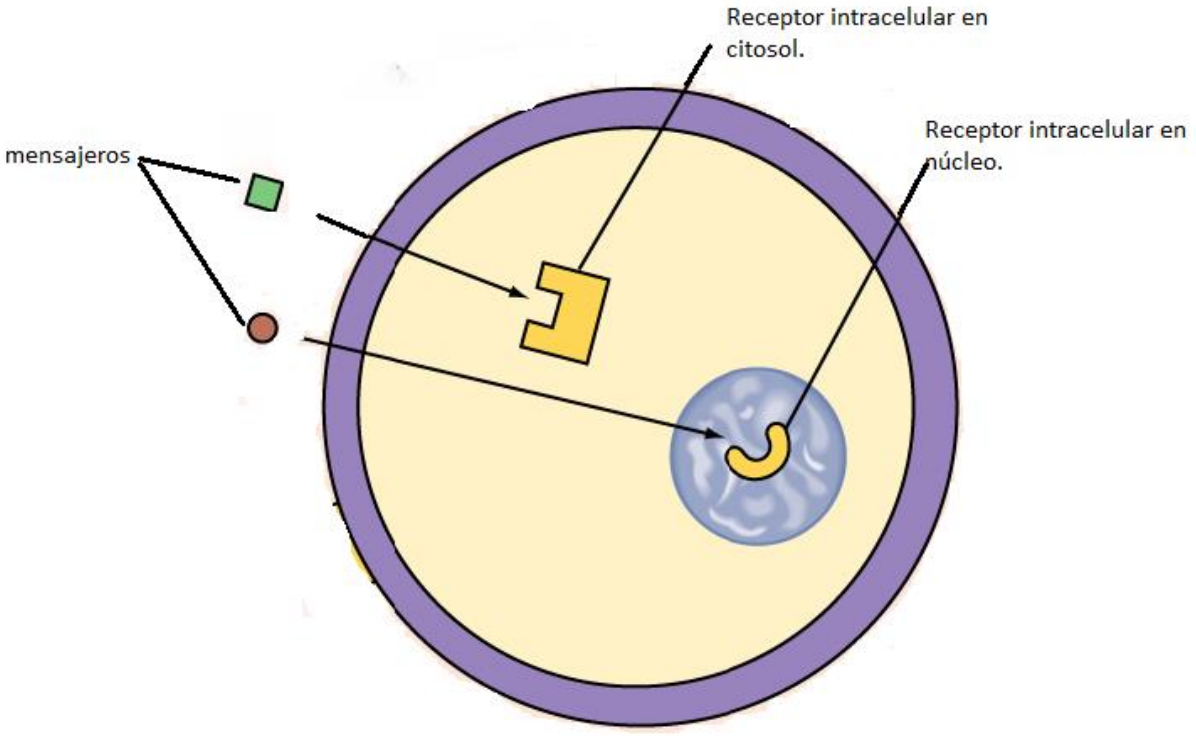


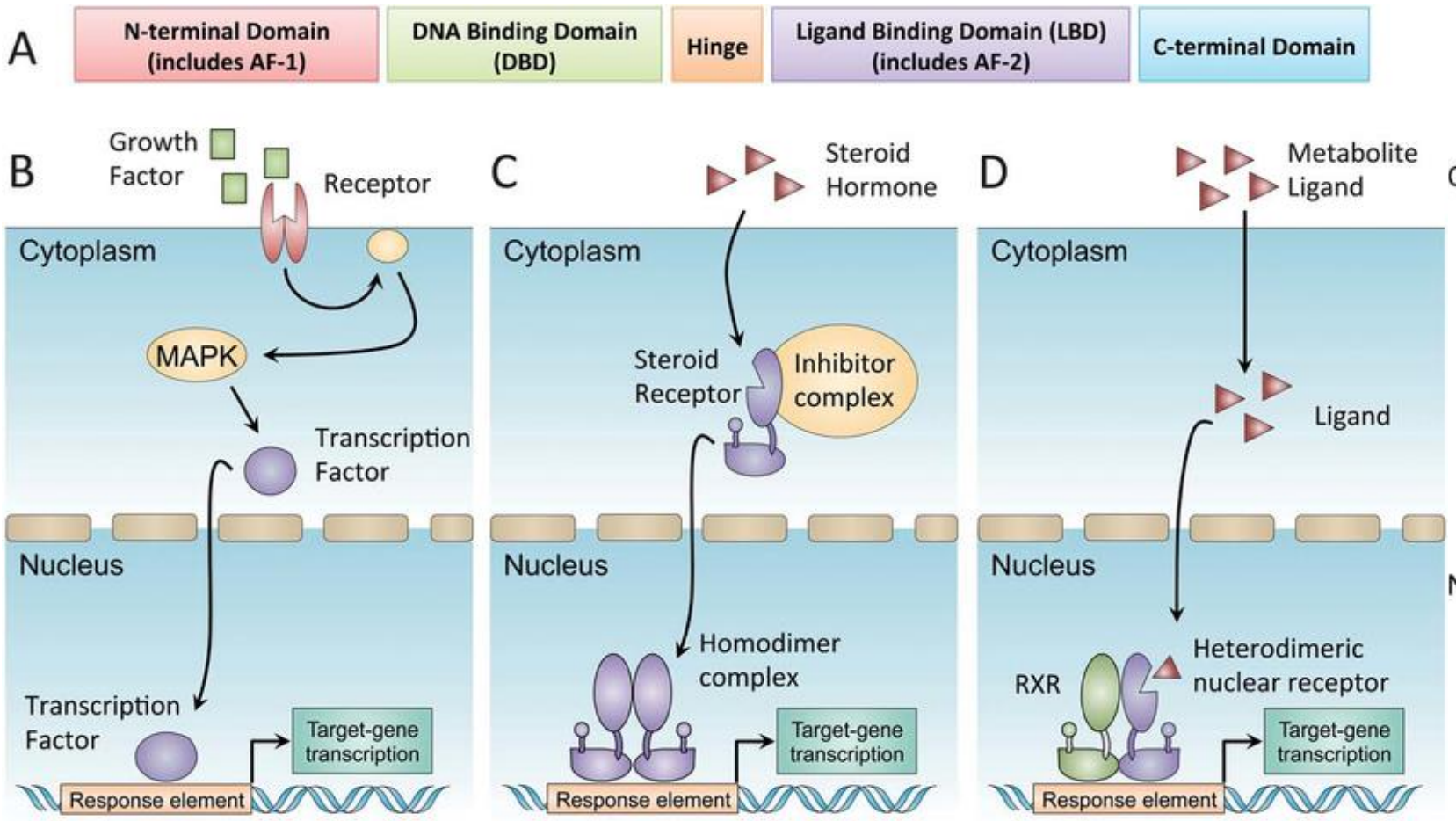


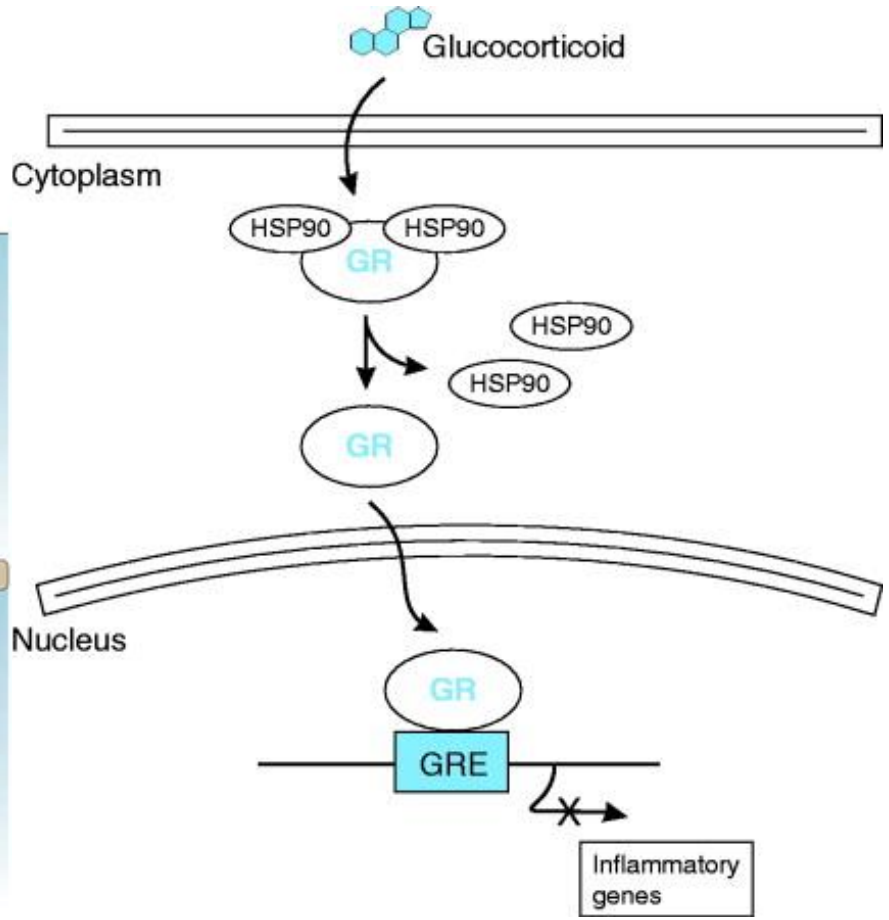

A RECEPTOR GUANYLYL CYCLASES
B RECEPTOR SERINE/ THREONINE KINASES
C RECEPTOR TYROSINE KINASES (RTKs)
D TYROSINE-KINASE–ASSOCIATED RECEPTORS
E RECEPTOR TYROSINE PHOSPHATASES
Extracellular space
N
C
Guanylyl cyclase domains
Cytosol
ANP RECEPTOR
Ligand
Serine-threonine kinase domain
Type I
Type II
TGF-β RECEPTOR
This is the kinase that phosphorylates downstream effectors.
Tyrosine kinase domains
NGF RECEPTOR
JAK2
Tyrosine kinases
GROWTH HORMONE RECEPTOR
Carbohydrate groups
Tyrosine phosphatase domain
CD45

Receptores intracelulares o tipo esteroide

- En el citosol o en el núcleo
- Son factores de transcripción que se activan por unión al ligando
- Relacionan señales extracelulares con transcripción genética

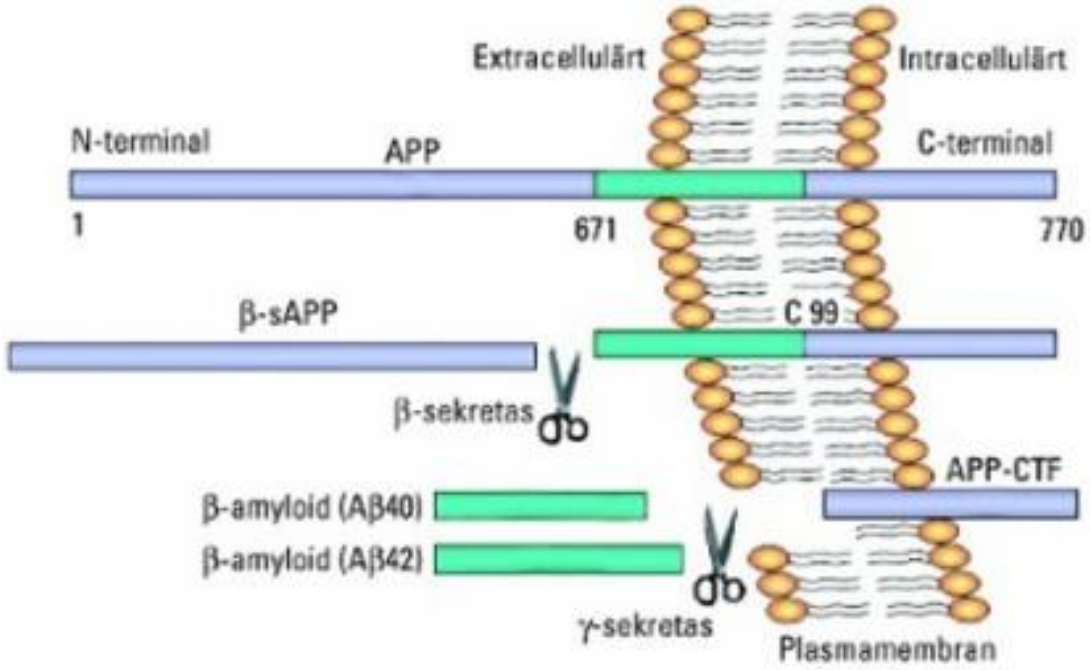


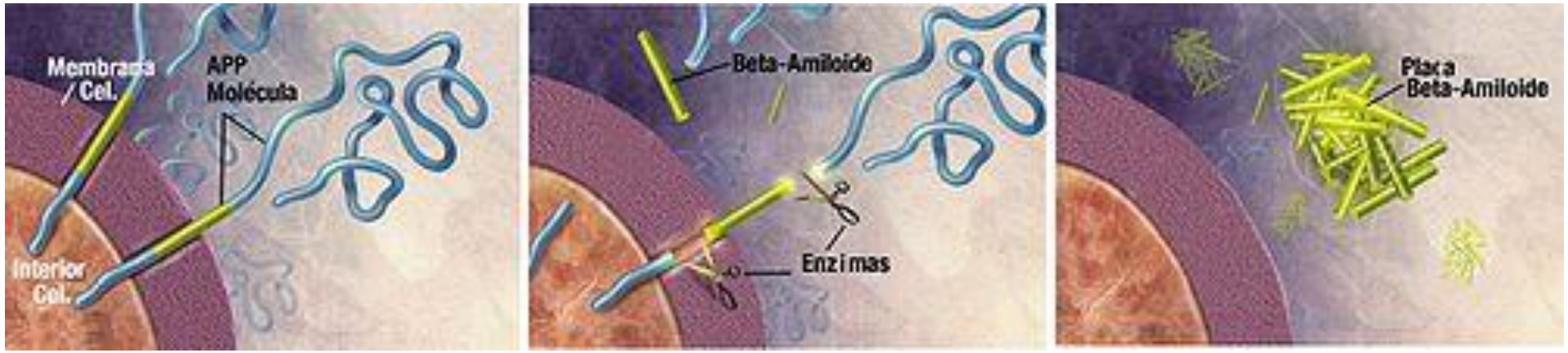

A
N-terminal Domain (includes AF-1)
DNA Binding Domain (DBD)
Hinge
Ligand Binding Domain (LBD) (includes AF-2)
C-terminal Domain
B
Growth Factor
Receptor
Cytoplasm
MAPK
Transcription Factor
Nucleus
Transcription Factor
Target-gene transcription
Response element
C
Steroid Hormone
Cytoplasm
Steroid Receptor
Inhibitor complex
Nucleus
Homodimer complex
Target-gene transcription
Response element
D
Metabolite Ligand
Cytoplasm
Ligand
Nucleus
RXR
Heterodimeric nuclear receptor
Target-gene transcription
Response element

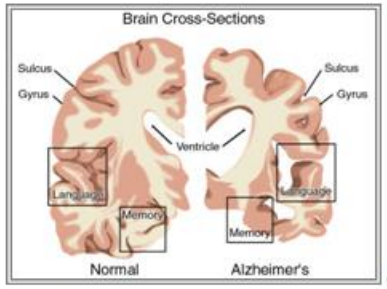

Glucocorticoid
Cytoplasm
HSP90
HSP90
GR
HSP90
HSP90
GR
Nucleus
GR
GRE
Inflammatory genes

Proteínas transmembrana que liberan factores de transcripción

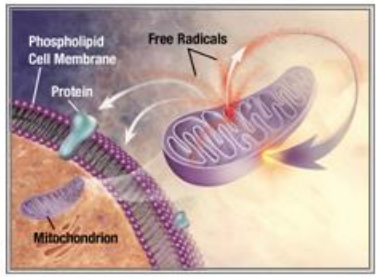
- Proteínas transmembrana que sufren un corte autocatalítico en la membrana, liberando fragmentos que entran al núcleo y modulan la expresión genética





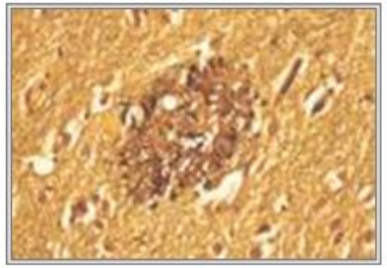


Pérdida de neuronas colinérgicas



Estrés oxidativo

Enfermedad de Alzheimer

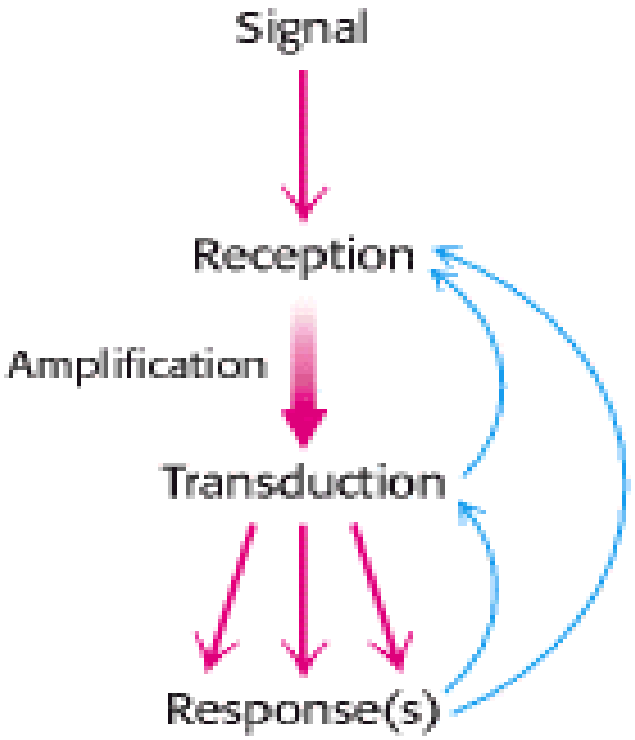


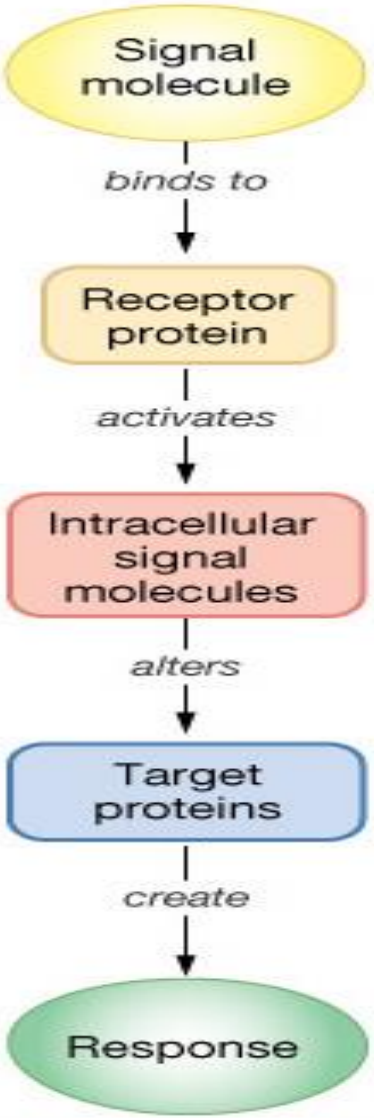
Placas de beta-amiloide

Ovillos neurofibrilares (Tau hiperfosforilada)

Eventos

- Reconocimiento
- Transducción
- Transmisión
- Modulación del efector
- Respuesta
- Terminación





Características de la transducción de señal

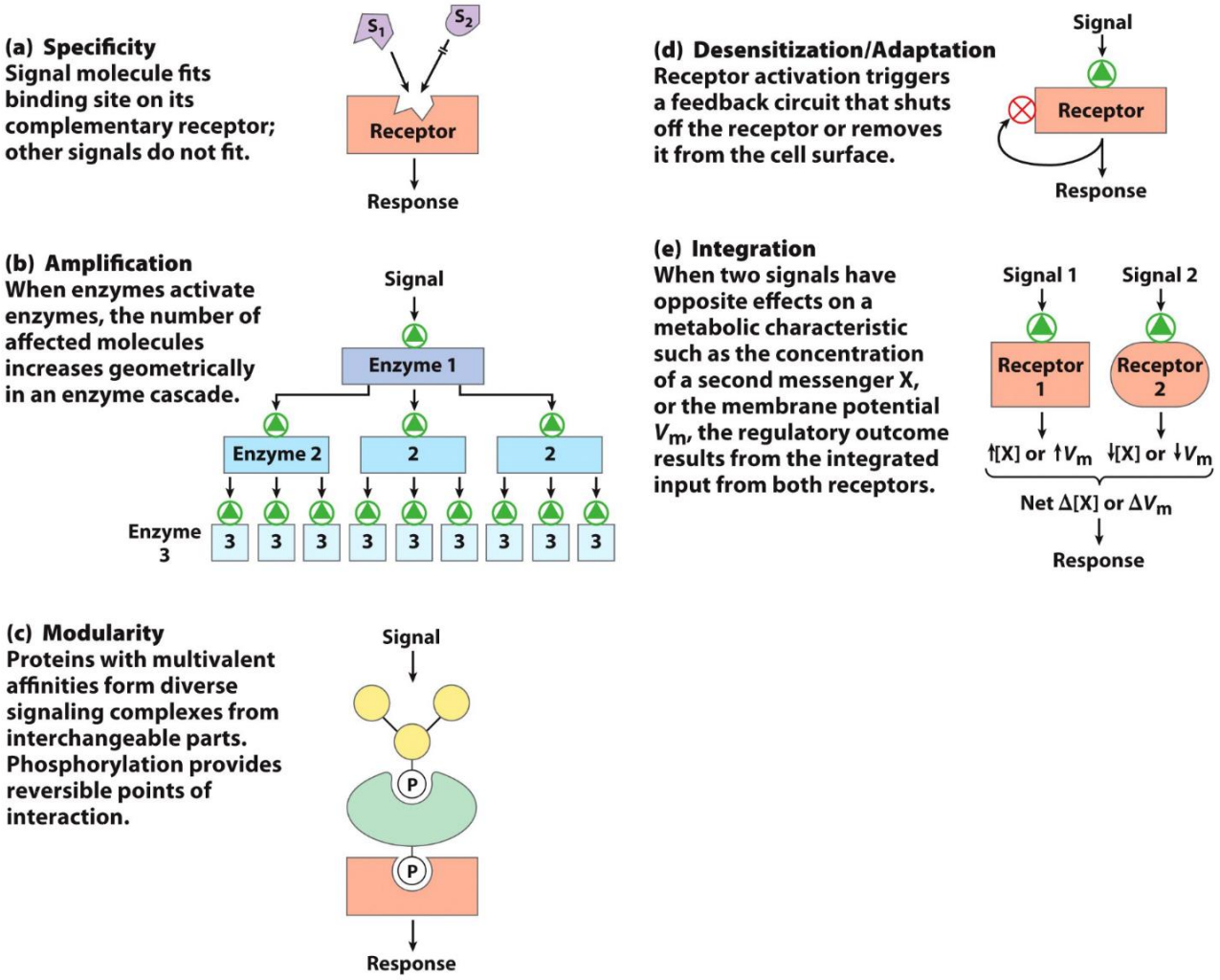


Figure 12-1
Lehninger Principles of Biochemistry, Sixth Edition
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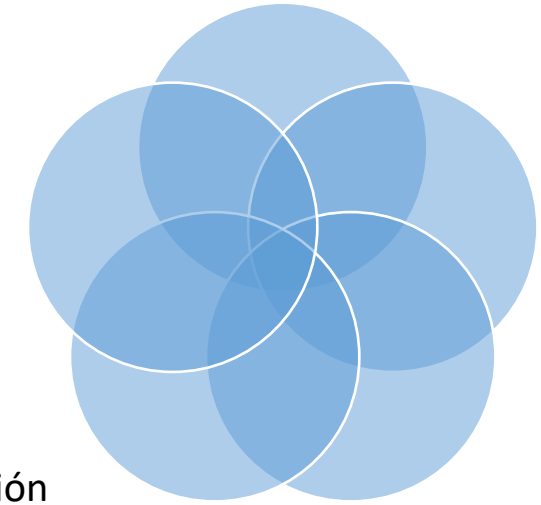
Especificidad

Integración

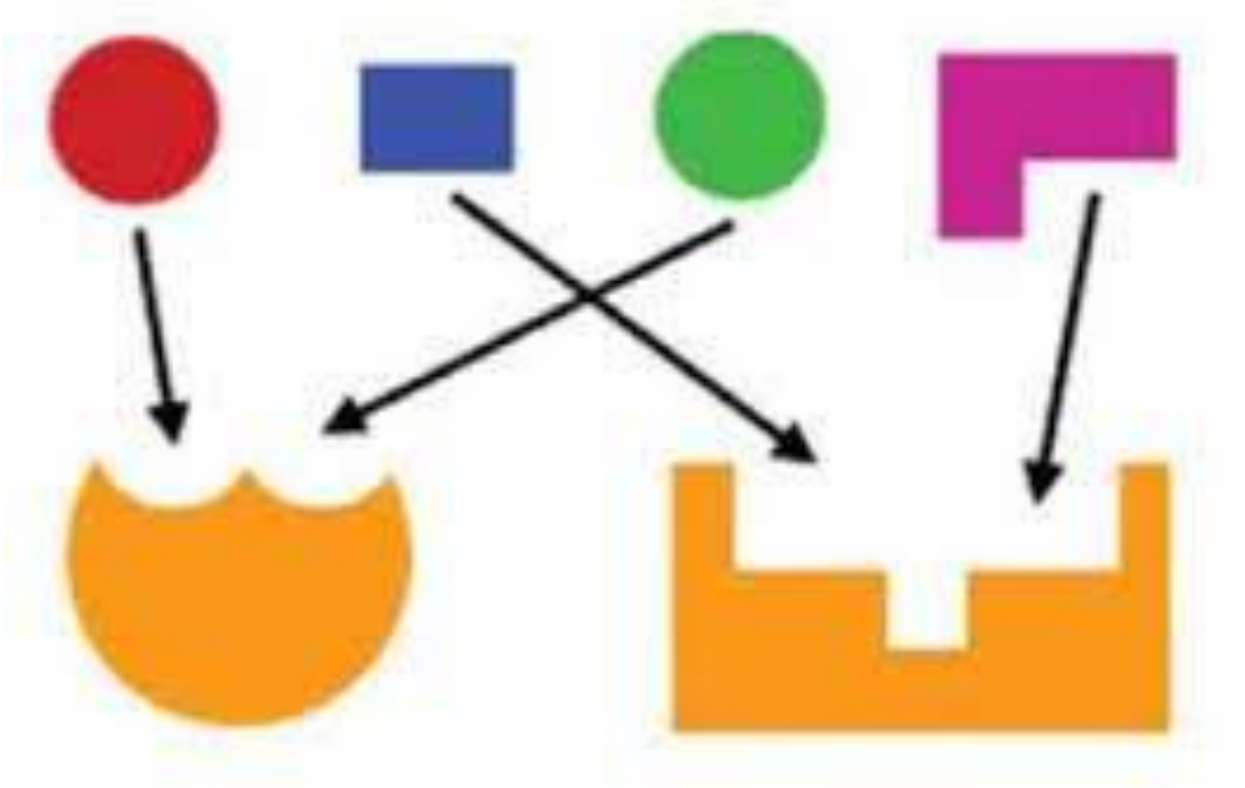


Sensibilidad

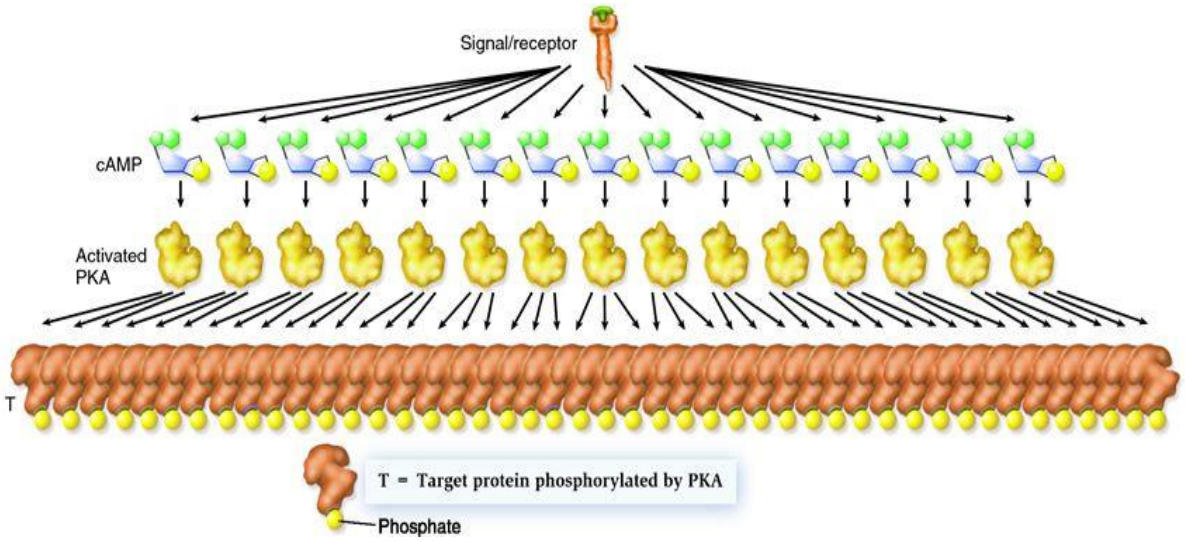
Desensibilización

Modularidad

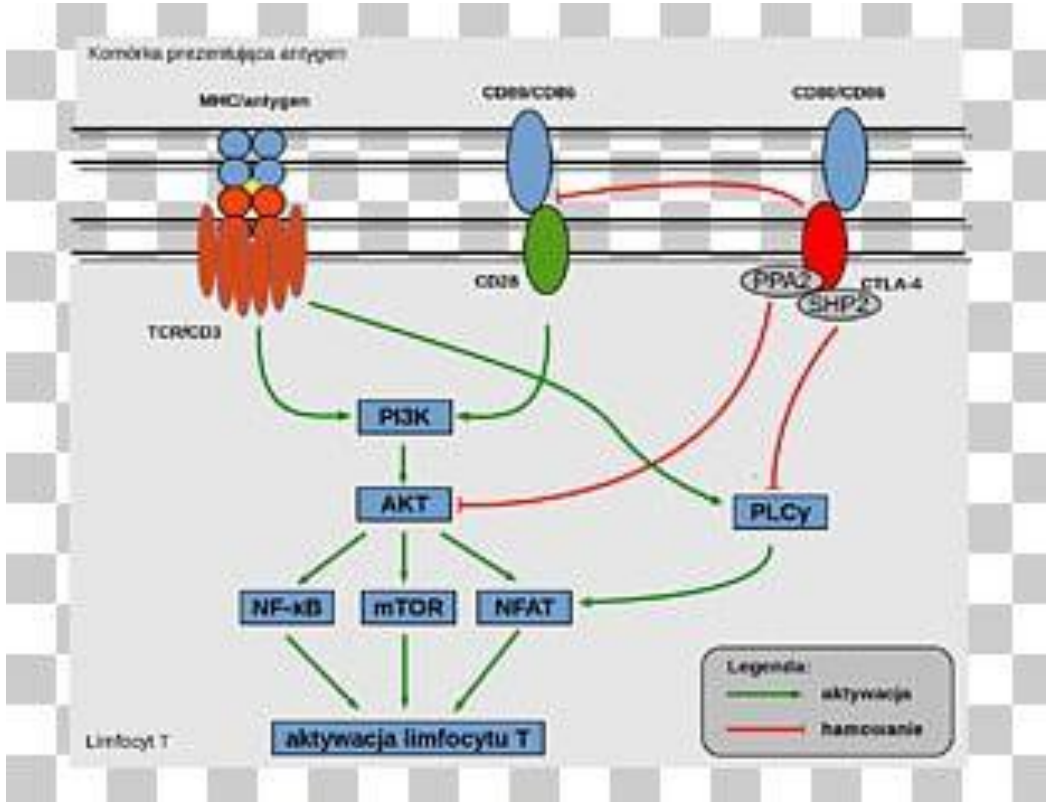
Especificidad



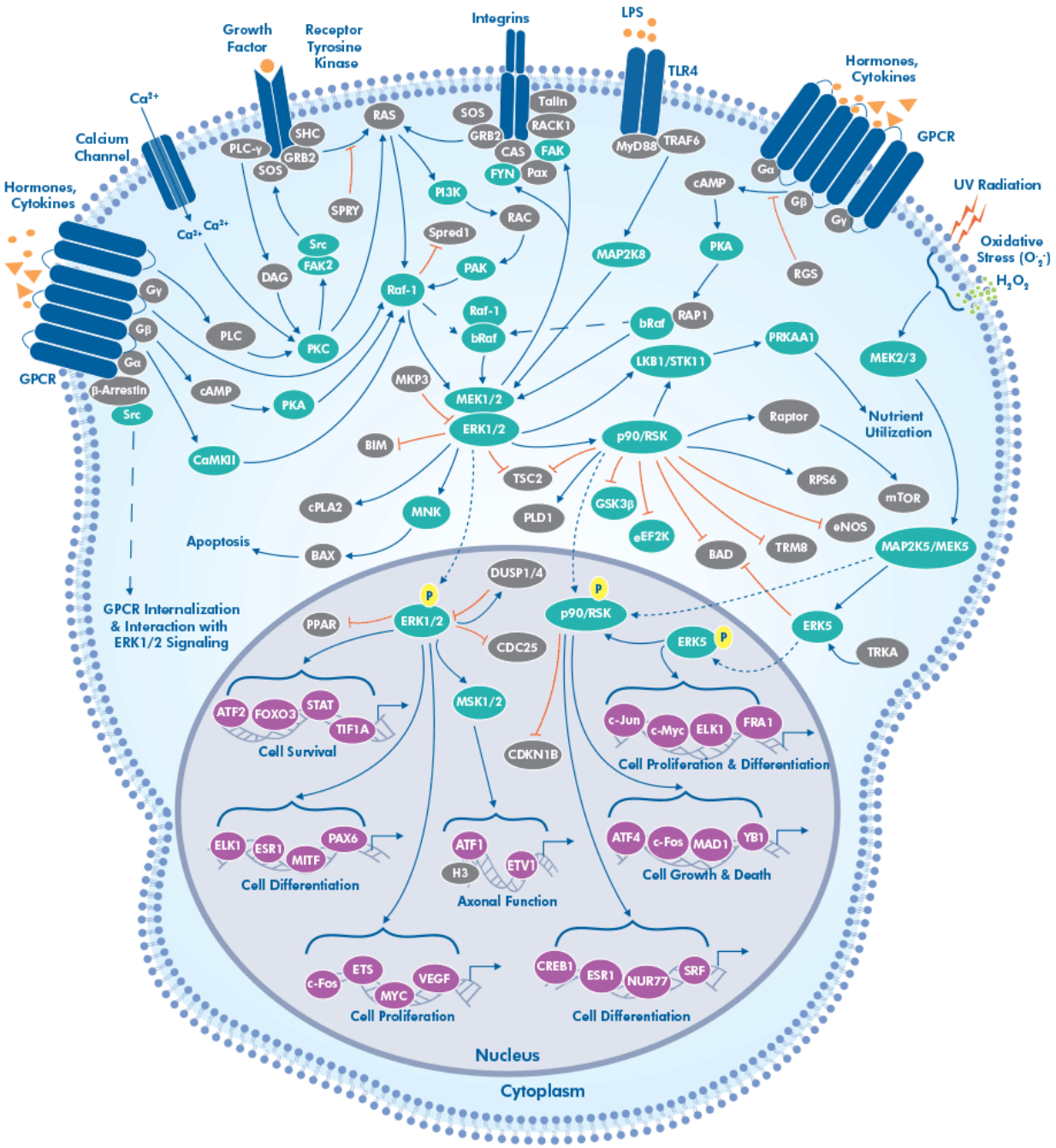
Sensibilidad



Modularidad



Ejemplo: MAPKs



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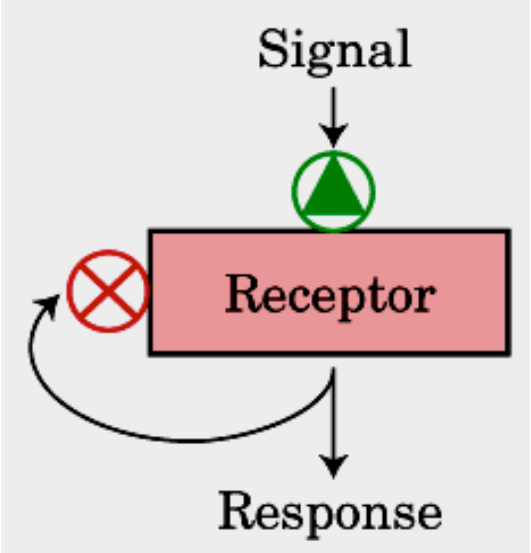
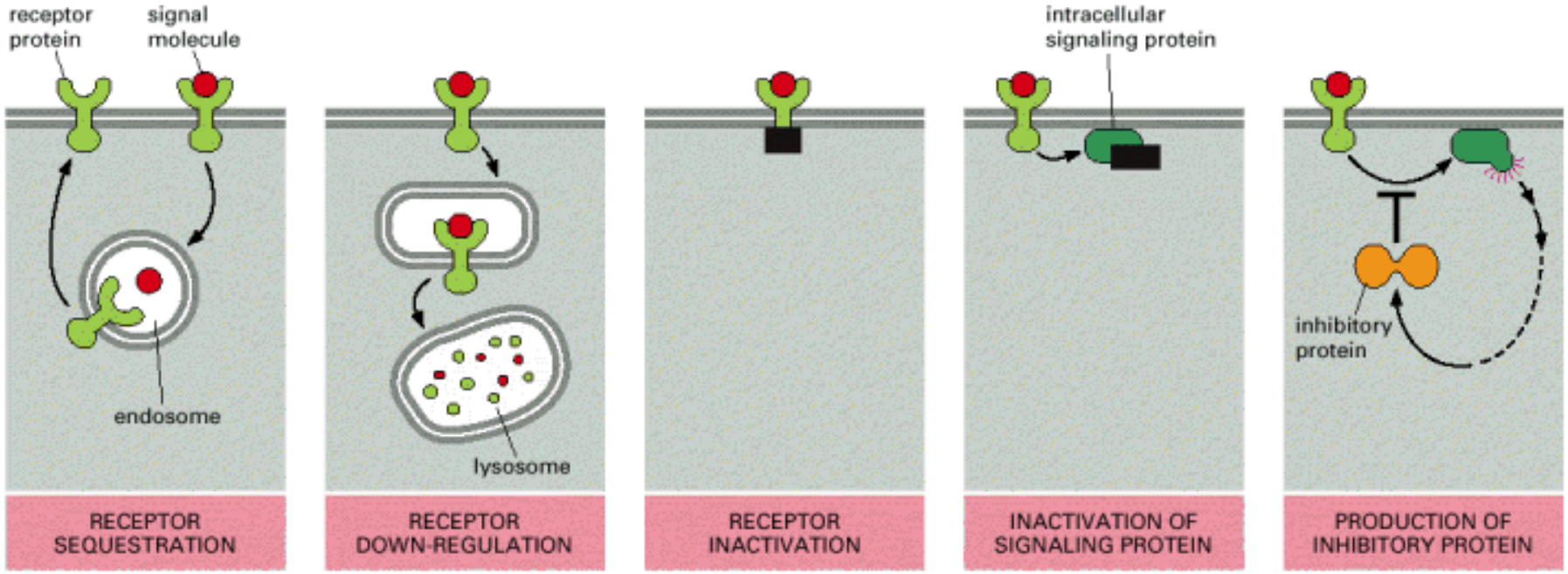
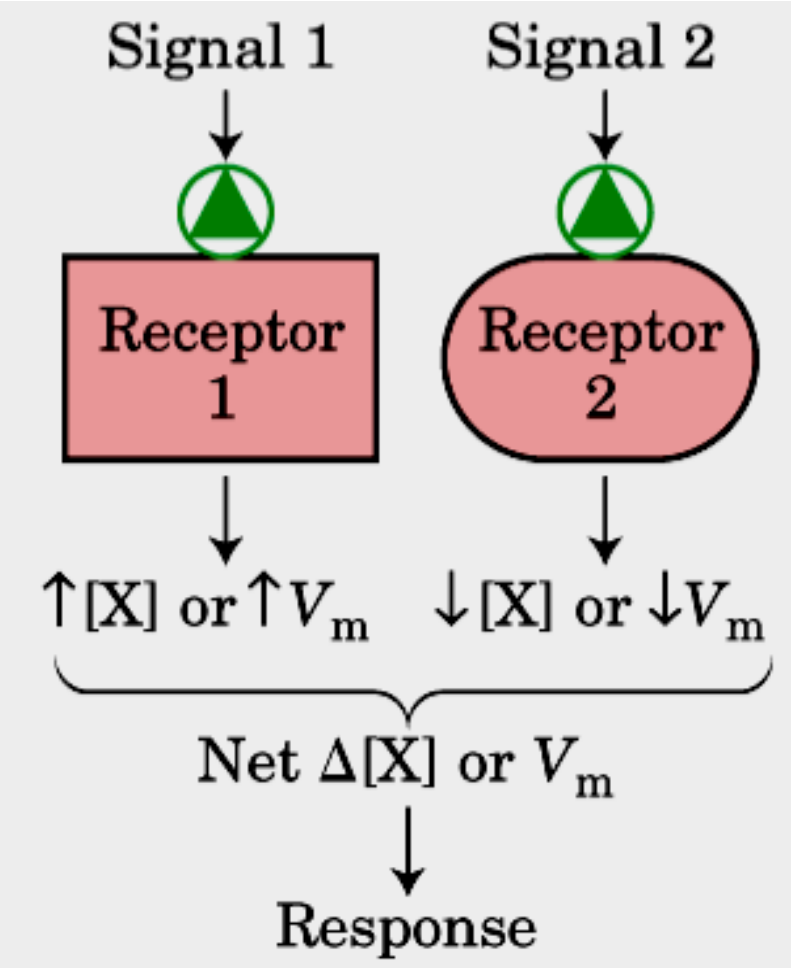
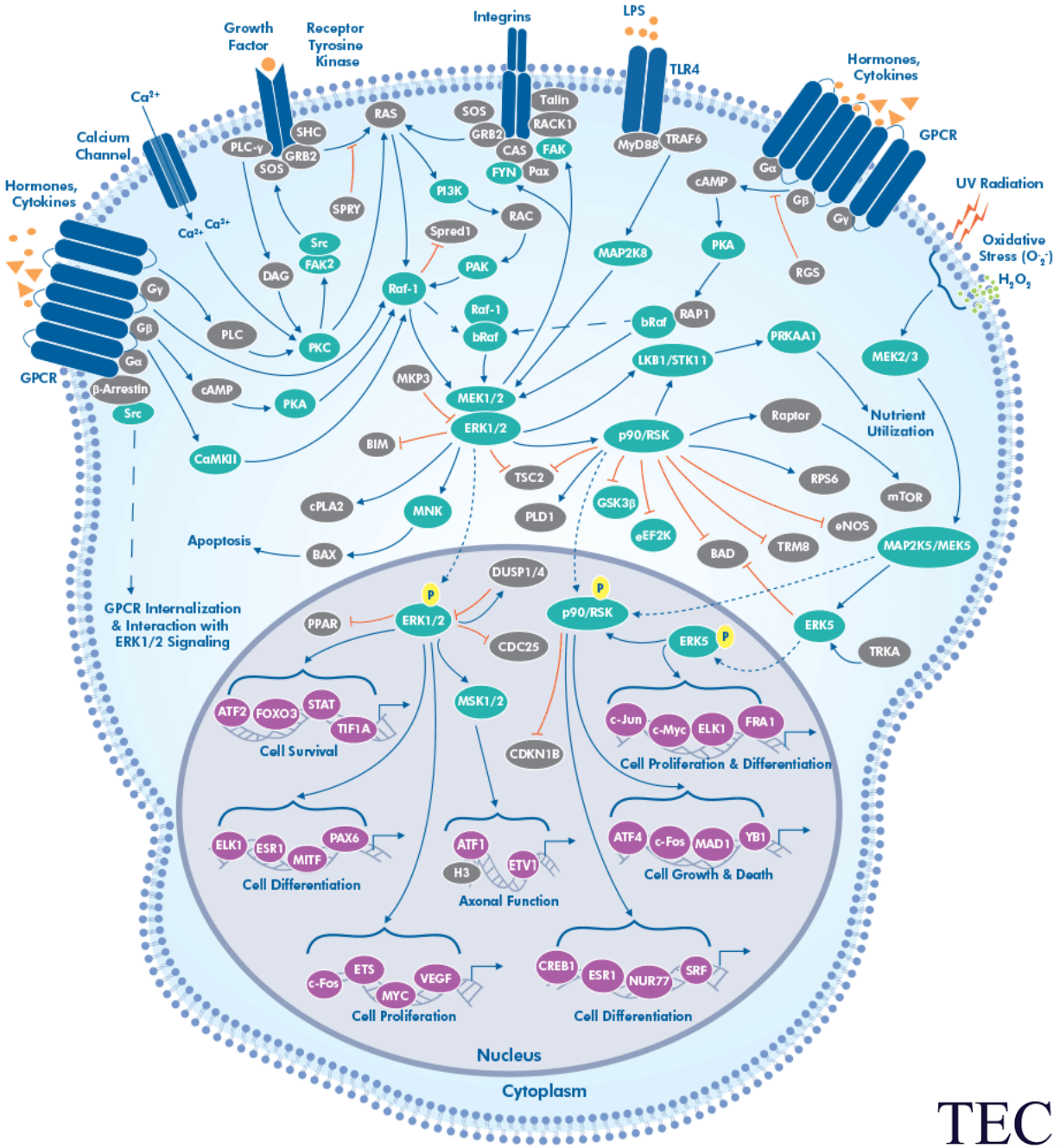
Desensibilización / Adaptación





Integración





Importante: La señalización no es linear, “Think of signal transduction as a web not a line . . .”

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Conversemos:

- Cuáles moléculas son ejemplos de “primeros mensajeros”?
- Cuáles moléculas son ejemplos de “segundos mensajeros”?
- Qué caracteriza a cada tipo de molécula?
- Por qué es importante que existan estos tipos de comunicación?
- Qué tipo de respuesta / regulación implica cada uno?